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The Bristol Medico-Chirurgical Journal

" Scire est nescire, nisi id me Scire alius sciret."

WINTER, 1933.

THE TWENTY-SECOND LONG FOX MEMORIAL LECTURE:

DELIVERED IN THE UNIVERSITY OF BRISTOL ON NOVEMBER 7TH, 1933.

THE VICE-CHANCELLOR (Dr. T. LOVEDAY, M.A., LL.D.) *in the Chair.*

BY

CECIL A. JOLL, M.D., M.S., F.R.C.S.,

Senior Surgeon to the Royal Free Hospital; Surgeon to the Cancer Hospital,

ON

RECENT ADVANCES IN THE ÆTIOLOGY, DIAGNOSIS AND TREATMENT OF CANCER.

THE Bristol Medical School has always had its great teachers, so that something more than the capacity to instruct must account for the outstanding position which Long Fox held in the medical world for over a quarter of a century. A fine character, combined with a striking personality, formed the basis of a

reputation which had made his name famous in the West Country when I was a schoolboy, and has so endured that to-day we meet to do honour once again to his memory.

ÆTIOLOGY.

Broadly, it may be said that there are two main hypotheses as to the real nature of cancer and the cancerous process: one, that it is a single disease comparable, for example, to syphilis; the other, that it is a complex of diseases, some as obviously closely related to one another as are the various species of a genus in some homogeneous natural order of plants or animals, others as obscurely connected as are certain natural orders themselves.

It follows that those who hold the former view expect to be able to find a single causative factor for cancer, and that in time a universal diagnostic method will be forthcoming which will reveal each and every malignant growth at its earliest stage. The logical outcome, it is assumed, would then follow, that is, a cure equally lethal for all types of neoplasm. Those who accept the latter hypothesis are prepared to find that progress in our knowledge of cancer is made bit by bit, rather than by any dramatic achievement which, at a bound, would justify our hopes of bringing malignant neoplasia into the category of a controllable disease.

Twenty years spent in intimate association with the natural history of the cancer problem, particularly in its clinical and pathological aspects, has converted me to the second of the alternative hypotheses, and thus I am compelled to be critical—I hope not hypercritical—towards the claims to diagnose cancer by a single test or to cure it by a specific agent.

In the endeavour to appraise progress in our knowledge of the causation of cancer one is at once impressed by the tendency to confuse the exciting cause — the "causa causans" — with the disease phenomena.

Thus it appears to me a fundamental error to attribute cancer, as did Farmer, Moore and Walker,[1] to sex-cell mitosis or to this or that peculiarity of the chromosome or nuclear material; one and all—even if it could be proved that they occur in every malignant growth — they are merely the cytological phenomena of the disease, and not its cause. A similar criticism must apply to Sampson Handley's[2] thesis that chronic lymph-stasis is the fundamental factor in carcinogenesis. He maintains that all carcinomata are preceded by papillomata, which are themselves the outcome of lymph stasis induced by chronic inflammation in the papillary lymphatics. No evidence, however, is brought forward of a similar cause for sarcomata, yet, as I shall show later, both carcinoma and sarcoma can be induced by the same carcinogenic compound. It is, moreover, extremely unlikely that there is any radical difference in the mode of action of such compounds on epithelial and connective tissues respectively. Handley's carefully considered and lucid thesis must be recognized as throwing a valuable side-light on the histology of the cancer process, but in no real sense clarifying the vexed question of its causation.

The skill of the bacteriologist and the pathologist have been fully tested by those who believe that cancer is comparable with a micro-organismal or parasitic disease, but I need not remind you that not one of the numerous theories in this group has withstood destructive criticism. It is, of course, true that Gye and Purdy[3] have made out a strong case for the belief that the Rous sarcoma of fowls is transmitted by a filtrable virus, the growths appearing extremely rapidly after inoculation. Nothing comparable with this is found in any mammalian cancer, and up to now Rous's sarcoma is to be classed merely as an interesting anomaly among neoplasms.

It is well established that certain metazoan parasites are capable of behaving as carcinogenic agents. Well-authenticated examples of this association are carcinoma of the stomach in

rats, which Fibiger[4] so brilliantly established to be due to a nematode (Spiroptera) carried to the stomach wall by a particular cockroach, and a sarcomatous tumour of the liver in rabbits produced by a cysticercus and carcinoma of the equine testis caused by a nematode. It must also be remembered that malignant disease at certain sites, and in particular animals, may in fact be due to a unicellular protozoan, the best known being the adeno-carcinoma of the liver of the rabbit in association with coccidiosis. Not one of these parasites should, I think, be regarded in any other light than as a carcinogenic agent comparable to the various physical and chemical agents which I shall shortly proceed to discuss.

Clinicians have for many years maintained that cancer frequently arises at sites liable to what they term "chronic irritation." I give you the term, as lawyers would say, "without prejudice," since there is no unanimity among pathologists as to whether in fact the change preceding the development of cancer at such sites actually is of a chronic inflammatory type. Furthermore, it must not be forgotten that many chemical irritants exist, *e.g.* chromic acid, which produce industrial skin diseases but do not lead to epithelioma. In recent years, too, there have been recorded many cases of cancer ascribed to the action of heat (Kangri burns), sunlight, X-rays, radium,[5] coal tar, paraffin and lubricating oils, aniline dyes,[6] arsenic and betel-nut.

Experimentally, the whole subject of carcinogenetic agents received a great stimulus by the discovery of Yamagiwa and Ichikawa[7] in 1914 that epithelioma can be produced by painting the ear of the rabbit with coal-tar. After the War a considerable series of positive results were obtained, chiefly in mice and rats, by a variety of other agents—radium,[8] X-rays,[9] ultra-violet light,[10] sunlight,*

* International Cancer Congress, Madrid, 1933.

dental tartar,[11] printing ink,[12] CO_2 snow,[13] paraffin,[14] folliculin.*

It is to be noted specially that in all cases the interval which elapses between the initiation of the use of the agent and the appearance of the tumour is considerable, relative to the life of the animal concerned. This is in strict accordance with the findings in industrial cancer, in which the interval is seldom less than ten and may be as much as fifty years. Leitch[15] has stated that in experimental tar-carcinogenesis there is the same incubation period whatever the age of the animal, and this is largely borne out by statistical inquiries in occupational cancer, as it occurs in aniline and tar workers, etc. It is of interest also to note that not only does a diet of liver increase the growth in tar cancers (Maisin and François[16]), but it also accelerates their appearance (Watson[17]).

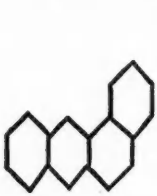
During the last few years a series of brilliant researches aimed at elucidating the problems of tar-carcinogenesis has been brought to fruition at the Research Institute of the Cancer Hospital, and it would be difficult to exaggerate their importance. The full details of this work are too technical for me to attempt to describe, but as an example of the value of team work in cancer research and of the great assistance which the cognate sciences can render to medicine, I feel justified in giving you a brief outline of this remarkable achievement.†

In 1927 Mayneord, while examining the fluorescence spectra of tar and shale oil, observed in them three very definite bands, one rather narrow and two wider near the limit of the visible rays. A systematic spectroscopic survey of various

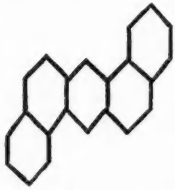
* Lacassagne, personal communication, 1933.

† I have to thank my colleague, Professor Kennaway,[18] Director of the Research Laboratories, for supplying much of the information relative to this part of my lecture.

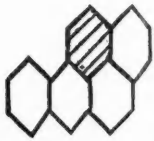
hydrocarbons next enabled him to detect a somewhat similar arrangement of bands in the spectrum of 1 : 2 benzanthracene,



1 : 2 benzanthracene.



1 : 2 : 5 : 6 benzanthracene.



1 : 2-Benzpyrene.

but this substance was found to be almost without cancerogenic powers. When, however, 1 : 2 : 5 : 6 benzanthracene was examined spectroscopically the bands were found to approximate still more closely to that of tar and shale-oil, and it proved to be strongly carcinogenic.

It was now realized that there were great possibilities along this line of investigation, and it was therefore attacked on a large scale. Hieger,[19] starting with two tons of tar, eventually obtained 50 grammes of a crystalline substance. This was found by Cook[20] to be 1 : 2 benzpyrene, a hitherto unknown substance. Cook[21] and Hewett[22] succeeded in synthesizing this compound and subsequently found that :—

1. Its spectrum is identical with that of tar and shale-oil.
2. It produces numerous growths, both carcinoma and sarcoma, in rats and mice.

Thus it has been established that an actively carcinogenic compound of known composition 1 : 2 benzpyrene occurs in tar and shale-oil, and is almost certainly the principal, if not the only active carcinogenic agent in them. (The other synthetic hydrocarbon, 1 : 2 : 5 : 6 benzanthracene, has never been *proved* to exist as such in tar and shale-oil.) More recently the same group of workers have synthesized two other actively carcinogenic compounds, viz. 5 : 6 cyclo-penteno—1 : 2 benzanthracene and 3 : 4 benzphenanthrene (chemically this latter is the simplest carcinogenic compound thus far known).

Further work is now being undertaken by Mayneord[23] to determine by spectroscopic methods, if possible, what types of molecular structures are concerned in the capacity of a

substance to induce cancer, and valuable information has also been obtained in this direction by the aid of X-ray crystallography in Sir W. Bragg's laboratory. When this is completed it may be possible to prove whether such substances as sterol and bile acids, occurring normally in the human body, could become converted under abnormal metabolic conditions into one or other of the carcinogenic hydrocarbons.

We know, for example, that the rut-producing hormone oestrin (or folliculin) is, chemically, probably an aromatic substance, and further, from the urine of pregnant mares an œstrogenic compound of the aromatic series can be isolated. Recently Lacassagne, of Paris, showed me cancers of the breast produced in male mice by fortnightly injections of folliculin, starting these injections when the mice were a week or two old. It is a remarkable fact, too, that 5 : 6 cyclo-penteno, 1 : 2 benzanthracene and 1 : 2 benzpyrene are not only carcinogenic but also œstrogenic.

Before passing on to discuss the hereditary factor in cancer it is, I think, proper to remind you that the identification of the carcinogenic substance in tar and shale-oil responsible for one type of industrial epithelioma emphasizes the probability of a multiplicity of causes of cancer, and helps to refute the claims of those who would ascribe cancer to a single cause.

Heredity.

Whatever may eventually be revealed as to the immediate exciting cause of cancer, nobody can be indifferent to the question: Is it inherited, and if so, under what circumstances? As practical clinicians we cannot fail to be impressed by the significance of heredity in connexion with disease and disease tendencies generally. By analogy, therefore, a strong case can be made out for an hereditary basis in malignant disease. The occurrence of certain tumours in identical twins provides a concrete example; thus H. Gideon Wells[24] records two such sets, all four of whom died of malignant disease of the testicle, the testicle affected and the histological structure of the tumour being identical in each twin. When, however,

an attempt is made to formulate the exact or even the approximate nature of the genetic influence in cancer production, we find ourselves at once involved in a problem of such complexity that up to now no single unassailable generalization on the subject has been evolved.

The careful experimental work of Slye,[25] continued as it has been over many generations in mice, led her to conclude that for certain spontaneous growths of the breast the tendency is for the disease to be inherited as a Mendelian recessive.

The unlikelihood of cancer-susceptibility being transmitted as a simple dominant was indicated by Tyzzer[26] as far back as 1907. He pointed out that if cancer were inherited as a single factor (or single gene) dominant, the crossing of an insusceptible individual with one homozygotic for cancer would result in the production of offspring in all of which the tumour character would appear. Such an occurrence, had it in fact ever happened, would certainly have been recognized clinically ere now. Little[27] has criticized Slye's conclusions severely, but without, I think, successfully refuting them *in so far as the particular type and site of the cancer* in Slye's series is concerned.

There is ample ground, however, for rejecting the idea that cancer, generally, is inherited in man as a simple recessive or simple dominant; but, nevertheless, there are one or two instances in human pathology in which malignant growths do indeed appear to be transmitted as simple gene dominants or simple gene recessives.

HUMAN TUMOURS TRANSMITTED AS MENDELIAN DOMINANTS.	HUMAN TUMOURS TRANSMITTED AS MENDELIAN RECESSIVES.
Retinoblastoma.	Malignant transformation of Xeroderma pigmentosum.
Multiple Neurofibromata.	Subcutaneous Lipomata (sex-linked).
Multiple Adenomata (polyposis of colon).	

These and a few others comprise all the tumours which appear to be inherited by simple genes, and it therefore seems to be more reasonable, as Haldane[28] suggests, that the genetical predisposition to malignant disease should be ascribed to multiple dominant genes.

It is, however, I think, fair to state that the investigations of the past twenty years indicate that cancer or, rather, cancer-susceptibility in man is undoubtedly inherited, but that no facts are available at present which make it feasible to minimize this susceptibility by any form of selective breeding such as is included under the term "eugenics."

In concluding this section of my lecture it should be put on record that as our knowledge of the natural history of cancer widens, particularly with regard to the occurrence of spontaneous tumours in wild and domesticated animals and among the less accessible races of mankind, more and more evidence is accumulating that race, religion, diet, moderate indulgence in alcohol or tobacco have no influence whatsoever on the causation of cancer. The refutation thus afforded of the loudly-proclaimed hypotheses of quacks, charlatans and fanatics may perhaps in time aid in checking the spate of fantastic suggestions, which serve only to confuse the issue in the minds of the general public while providing fresh material for exploitation by the sensational press.

DIAGNOSIS.

Few will quarrel with the statement that success in cancer therapy lies in the earliest possible diagnosis. One of my lay friends has expressed this rather aptly, I think, in the slogan : "Fear not cancer, fear delay." Those of us who are actively engaged in treating

malignant disease have opportunities daily to witness the tragedy of procrastination on the part of the patient, and not always the poor and ignorant one; but this is not the whole story. As a profession we are not yet sufficiently tuned up to be constantly suspicious of the existence of cancer. I have tried to avoid thus far the appeal to statistics to illustrate my points, but here it seems to be inevitable. Fortunately, they are relatively simple and unequivocal.

MacCarty[29] reports that from 30 per cent. to 50 per cent. of all cases of cancer of the breast seen at the Mayo Clinic over a period of years were inoperable at their first examination, the figures for the large bowel and stomach being 42 per cent. and 75 per cent. respectively. My own experience fully confirms these statistics, except in connexion with carcinoma of the stomach, in which during the last twelve years less than 20 per cent. have proved operable, the tendency recently being, I regret to say, for the percentage to fall rather than rise, the direct outcome, I believe, of the misguided enthusiasm for the alkaline treatment of all forms of dyspepsia. Only when the lesion has unmistakably declared itself as malignant is the diagnosis of simple gastric ulcer abandoned. MacCarty states further that less than 25 per cent. of the cases of gastric and colic cancer had been X-rayed before reaching the Clinic, and 20 per cent. of the rectal and sigmoid growths had shortly before been treated for such conditions as piles and fissure in ano and the malignant lesion entirely overlooked.

De Vries,[30] of Amsterdam, found that 20 per cent. of cancer cases had not been recognized previous to autopsy, and conversely 10 per cent. diagnosed as cancer were found free from malignant disease. Closely comparable figures are provided by the Imperial Cancer Research Commission[31] in England and by Bilz[32] in Germany. Naturally, the greater percentage of errors occurred in connexion with deep-seated growths, but it must be obvious that as the figures relate to autopsy material, presumably the percentage error at the earlier stages is very much higher.

It is also significant that Reimann and Safford,[33] surveying 3,780 cases of cancer over a period of twenty-eight years, could

find little evidence of improvement in the delay in seeking proper advice, even towards the end of the period.

It is impossible to face these facts without concluding that we are not educating our students and practitioners to suspect cancer often enough. It must be borne in mind that the number of cases of malignant disease met with by a general practitioner is relatively small; for if we assume that 75,000 cases occur per annum, and that there are 25,000 doctors in general practice in this country, this gives an annual average of three cases apiece. Unless, therefore, the student of medicine, undergraduate or graduate, receives special instruction in the diagnosis of cancer and is given opportunities for the periodical revision of his knowledge, little progress will be made, however great the resources available in the hands of the trained cancer expert. It is useless to equip a factory with the most modern machinery if the appropriate raw material is lacking. Universities with medical schools and the special cancer hospitals must stimulate and organize courses for the instruction of students, and, on the other hand, medical men must show themselves more eager to benefit from the facilities for the study of cancer which already exist in the large centres of learning. If any doubt should still remain in your minds as to the extent to which delay in diagnosis influences the successful treatment of malignant disease, I commend you to the study of a most valuable and instructive series of reports by Dr. Lane Clayton[34] and others, issued under the auspices of the Ministry of Health during the last ten years.

Those who believe in the "unity" of the cancer problem naturally seek to find a solution for all diagnostic problems in a single test applicable to

every type of malignant disease even at the earliest stage. If such a test were forthcoming its value would undoubtedly be great, and the discoverer would deserve to rank with Pasteur and Lister; but it is inherently most unlikely that a test of this kind could establish at once the site, size, histological structure, grade of virulence and radio-sensitivity of the growth, yet without a knowledge of all these the diagnosis must always be rated as imperfect.

Many attempts to provide such a universal diagnostic test for cancer have been made during recent years, and several of them have yielded a considerable percentage of accurate findings. Most of these tests rely on the assumption that the malignant cell adds certain abnormal substances to the blood-serum, or that these abnormal substances are produced by the body cells in response to the presence of the cancer cells.

Shaw-Mackenzie[35] was among the pioneers of such diagnostic tests. He maintained that in cancerous states the serum co-enzyme is decreased and, conversely, after removal of the growth it is increased, only to fall again in cases of recurrence. It is, however, only right to point out that the test has been severely criticized, especially when "positive." Normal healthy people, and those suffering from non-malignant diseases, often yield "positive" reactions to this test, and, in fact, whenever the fat-content of the serum is over 0·2 per cent. a positive reaction is found. When "negative" the test would appear to indicate that it is about four chances to one that cancer is absent, though Shaw-Mackenzie claimed a 95 per cent. accuracy for the test.

More recently modifications of the Abderhalden immunity reaction have been investigated with a view to establishing a reaction comparable to that of Wassermann. My colleague, the late Dr. H. J. B. Fry,[36] recorded in 1925 the results of such an investigation. He employed antigen from breast tumours, and his results accorded with the clinical and

histological diagnosis in 75 per cent. of cases. Curiously enough, the diagnostic accuracy was higher for the more deeply-seated growths (such as those of the bowel) than for those of the skin. In sarcomata the index of accuracy was 86 per cent. As with Shaw-Mackenzie's test, a "positive" result was often obtained in other diseases, *e.g.* in febrile conditions and tuberculosis. Others have employed methods based upon the same principles, though modified in detail, but none of them has yielded a sufficiently high standard of accuracy to justify its employment as a diagnostic criterion warranting routine application.

There is another test which has been employed in various modifications by several observers based on the changes in the serum proteins which have been described as occurring in malignant disease. The Kahn,[37] Bendien,[38] Schmitz and Wulkow[39] tests are all dependent upon various methods of estimating the globulin-fraction in the blood-serum. It is fairly generally conceded that in about 80 per cent. of cases of cancer there is a demonstrable rise in the percentage of globulin in the blood-serum, but unfortunately an equally striking rise may occur in certain diseases in no way related to neoplasia, and it was this fact that was overlooked when Bendien's test was being checked a year or two ago. Great hopes were raised because a high degree of accuracy was reached in distinguishing the sera in cases of malignant disease from those of healthy controls, until it was realized that the test failed to differentiate between persons suffering from cancer and those the subject of certain serious (but not cancerous) diseases. Freeman[40] and his co-workers, and Smith, Holiday and Marrack[41] have demonstrated the futility of Bendien's method as originally described, not only in the respect of the flocculation factor, but also of the spectrographic examination of the precipitated proteids, but recently Cronin Lowe[42] has claimed a very high degree of accuracy for his own modification of Bendien's method.

In 600 unselected cases he calculates that the percentage error is only 4·25, and states that although pregnant women often give a positive reaction, he has good ground for regarding the method as reliable, not only as a qualitative test for malignant disease, but also quantitatively, as an indication of a rapidly-advancing case, or of a recurrence after treatment. This work has not been confirmed by any independent observer;

on the contrary, such information as I have gleaned on the matter is unfavourable. Therefore, in view of the fundamental weakness of all such tests (since they are so frequently found positive in diverse diseases), I should be surprised if it survives the test of time and further experience.

Although I have explained my reasons for doubting the value of any general laboratory test for cancer, there are certain specific types of malignant disease at specified sites which can be detected with certainty by particular tests. Thus in carcinoma of the testis the Ascheim-Zondek reaction is obtainable from the urine (Hady),[43] and in fact becomes negative with the removal of the growth and reappears if it recurs. Ferguson,[44] of the Memorial Hospital, New York, has similarly established the diagnostic and prognostic value of the presence of intermedin—the hormone of the *pars intermedia* of the hypophysis—in the blood-serum, in cases of neuro-fibromatosis, neuro-sarcoma and melanotic sarcoma. In connexion also with the rare disease multiple myelomatosis the discovery of the specific (Bence-Jones) protein in the urine is diagnostic (McIntyre[45]).

Limited as may be the value of all these tests, are we justified in taking a pessimistic view of cancer diagnosis in general? I think not. In the hands of those specially trained, diagnostic accuracy has been developed to the pitch that there are few cancers, however obscurely situated, which cannot be detected at any early stage, but in order to reach such high diagnostic standards the closest co-operation is needed between the various members of a team of experts working under the same roof. More—not less—centralization is required to ensure that facilities for the diagnosis of cancer, in the fullest sense of the term such as I have defined it earlier in this lecture,

should be available. The cancer clinician must be accustomed to recognizing every type of pre-cancerous lesion, must be an expert in detecting by palpation early malignant masses, capable of employing with precision laryngoscope, bronchoscope, œsophogoscope, yes, to-day, even the flexible gastroscope of Schindler and Wolff,[46] to say nothing of the gastric camera, the thoracoscope, cystoscope, sigmoidoscope and vaginal speculum, and last, but not least, he should be trained in the recognition of all forms of malignant disease by naked-eye examination of the tumour in bulk. His associate, the radiologist, must be able to visualize with the fluorescent screen the early indications of abnormality in the alimentary canal which suggest malignancy, to interpret the subtle modification of the contours of the renal tract revealed by excretion-urography, to detect the peculiar type of calcification associated with certain tumours of the brain, to give a correct opinion of the numerous types of bone tumour in respect of their radio-sensitivity, and in innumerable other ways to confirm, modify or correct the clinician's findings. The pathologist who forms the third leg of this essential diagnostic tripod must not only be able to give a correct opinion on the histological nature of a tumour, but ought to be capable of grading its malignancy and judging of its probable response to radiotherapy. Such a diagnostic team is the product of years of concentration and continuity of effort, it cannot be created by the edict of bureaucratic bodies, however powerful, and it can never be duplicated to the degree which would permit of more than a strictly limited number of diagnostic centres being formed for the whole country. In the absence of a highly-organized system of cancer diagnosis such as I have outlined, far

too much reliance tends to be placed on the examination of a portion of the tumour removed in an exploratory operation—the so-called biopsy.

The operation itself, unless conducted so that the whole tumour is removed with a reasonable margin of surrounding tissues, is liable to stimulate the growth or to cause its dissemination. The removal of a mere fragment of tissue may prove deceptive, the knife cut having failed to include any of the malignant cells. The portion excised may be so degenerate or atypical that an incorrect or doubtful opinion is arrived at. While, therefore, it is true that under favourable conditions the examination of biopsy material, both in the fresh state and after staining, may be occasionally helpful, we should rely more and more on a knowledge of gross pathology, and reserve biopsies for exceptional cases. When exploration is essential and the tumour deeply-seated, I prefer to use a fine hollow needle to obtain by aspiration the diagnostic material, rather than the usual open operation, and to give the pathologist all the time he needs for the examination rather than extract from him a hurried opinion. The soundest reason for a biopsy is that it enables the modern pathologist to grade the tumour according to the activity of its cells. This aspect of the diagnostic problem has not been as systematically pursued in this country as its merits deserve. I am satisfied that by using Broders'[47] grading method, which is based on the proportions of anaplastic and differentiated cells present, a more precise estimate of the potentialities of the tumour is obtained than by any mere qualitative description of the degree of malignancy of the tumour cells.

It ought not to be forgotten that the radio-therapeutist may be called on to aid us in cancer

diagnosis as well as in treatment. The reaction of a tumour to one or more deep X-ray therapeutic doses may well help to resolve the doubt in certain difficult cases. Thus, in connexion with bone tumours, it will serve to differentiate between the cellular endosteal sarcoma (which regresses after exposure to X-rays) and chronic osteomyelitis (which is aggravated by similar doses). Summing up, one may say that though there is no justification for complacency, in recent years as great or greater progress has been made in the diagnosis of cancer as in any branch of cancer knowledge.

TREATMENT.

Surgery.

Until early in the present century the scientific treatment of cancer was entirely governed by the development of surgical technique in response to the rapidly expanding knowledge of the pathology of neoplasms and their methods of dissemination. Thus, for cancer of the breast Stiles[48] and Handley[49] amplified and improved on the classical operation of Halstead, Crile[50] elaborated a method for extirpating secondary malignant cervical glands which has largely superseded that of Butlin, Miles[51] worked out a procedure for the resection of the malignant rectum which more fully fulfils the principles of surgical pathology than did Kraske's, Pólya[52] modified Billroth's form of gastrectomy and Wertheim[53] showed that it was possible to carry out a panhysterectomy in such a way as to conform to the surgical necessities of an infiltrating neoplasm of the cervix uteri, obtaining thereby many cures by purely surgical measures.

The notable successes of these surgical pioneers were not achieved without considerable mortality, to

say nothing of the inevitable mutilation, but this has not deterred their followers from practising even more extensive operations in the attempt to realize the great surgical ideal in cancer therapy, viz. to remove the primary tumour and all of its extensions in one mass, without at any stage cutting through tissue containing malignant cells. Improvement in anæsthesia has done much to aid the surgeons in their endeavours, but even before the Great War it was becoming clear that the scope of surgical operations for cancer had well-nigh reached the limit which the human body could withstand.

Surgery, indeed, still has the premier place in the treatment of most forms of cancer, particularly those affecting the stomach, bowel, breast and brain, but it no longer is the sole therapeutic method available. Radium therapy, X-ray therapy singly or combined, or either or both in conjunction with surgical measures, must be recognized as having a place in cancer treatment, and at certain sites, *e.g.* the cervix uteri, to have largely superseded purely surgical procedures.

Irradiation.

The revival of radium therapy, after its original eclipse, started little more than ten years ago, and in this country really systematic work on a large scale scarcely covers half that period, so that we are dependent to a great extent on the reports from Paris, Stockholm, and New York for most of the statistical information relating to the numbers of five to ten year survivals. Enough has been learnt, however, to cause us to emphasize the difficulties and dangers of radium therapy rather than the reverse, and to raise doubts as to the wisdom of endeavouring

to popularize this form of treatment by multiplying the number of hospitals and clinics where it can be applied. It is useless, or positively dangerous, for generous donors to supply institutions with large amounts of radium unless a trained staff of physicists, radium officers and technicians, pathologists and surgeons is available, to say nothing of the special buildings and plant which cannot be easily improvised.

The Radium Commission has so far wisely avoided this error by limiting the number of approved "National" centres to large towns with Universities or Medical Schools, but there are, unfortunately, many independent institutions where radium therapy is essayed without the necessary minimum personnel, and therefore unsatisfactory results are bound in the end to arise, and thus unjustly discredit this type of treatment.

Radio-sensitivity is now known to be the real basis of successful radium treatment. It is, however, still to some extent a matter of discussion as to what part is played in radio-sensitivity by the cancer cells themselves, by the reticulo-endothelial cells, and by the blood-vessels in and around the tumour cells respectively; but there is strong evidence that the macrophage is a very prominent factor in the production of favourable responses to gamma rays. It is also believed that the gamma rays are more effective in tumours the cells of which are actively dividing, or about to divide, and in those with a soft, vascular, delicate stroma.

Regaud and Lacassagne[54] have worked out the radio-sensitivity of a large number of normal tissues and of the cells of some neoplasms, but although this work has been amplified by others recently, we can still only speak in very general

terms of the radio-sensitivity of most neoplasms. Thus Haagensen[55] found in opposition to the law of Bergonié and Tribondeau, that in adenocarcinoma of the thyroid the most rapidly growing and anaplastic types were uniformly radio-resistant.

Closely related to the subject of radio-sensitivity is that of radium dosage, and this has been one of the greatest stumbling-blocks in radium therapy. The standards of dosage have, until recently, been milligram-hours or millicuries destroyed—neither of these methods has any real scientific or comparable value, but happily we are now rapidly approaching the stage when it will be possible to estimate dosage in standard *r*-units as now employed in deep X-ray therapy. Mayneord,[56] for example, has calculated that 1 mg.-hr. at one centimetre distance from a point source is approximately 9 *r*, and this figure has been confirmed in several ways by other observers. It has been customary in many centres to express the dose of gamma or X-rays in terms of the skin erythema dose (S.E.D.), but since this may be 50 per cent. more in the case of the scalp than elsewhere, and greater in skin poorly supplied with blood than it is in well-nourished skin areas,[57] it is obvious how urgent it is to provide a universal standard for gamma radiation, as has been done recently for X-radiation. I can only briefly refer to a few points in radium therapy which appear to me to represent important advances.

In employing the *interstitial method*, by "needling" or by "radon" seeds, there has been a tendency in certain clinics to increase the screenage from the more usual 0·5 mm. Platinum to 0·8 mm., and improved results are claimed in the avoidance of damage to cartilage and bone, the capacity to give more prolonged doses and in the actual benefits which follow.

With *surface applications* the main advance in recent years has been in the more accurate distribution of the radium so as to give a uniform dosage. The necessary calculations for this in connexion with plane surfaces have been carried out by Mayneord[58] and he is extending the work to surfaces of a more complicated form.

Beam Therapy.—On the Continent and in the Memorial Hospital, New York, "bombs" of four grammes or more have been in use for several years. In this country there has been little opportunity to use so large an amount. A 5-gramme unit

is, I am glad to say, to be set up immediately under the control of the Radium Beam Research Committee, and important developments are to be expected at the end of the two years' experimental period.

We have been using a 1-gramme unit successfully for some years at the Cancer Hospital, and others of this size are now being worked with at University College Hospital and at the Middlesex Hospital, while a 2-gramme bomb is employed at the Westminster Hospital. The great virtue of the " bomb " is that by adopting several " ports " of entry it is possible to deliver a depth-dose of uniform intensity to growths which are almost or quite inaccessible to other methods of radium therapy, and which are hardly within the realms of practical surgery.

I can only lightly touch on the triumphs of the gamma-ray treatment in cancer and the indications for its use. It is the best method of treating (with a view to cure) epithelioma of the skin, lip, mouth, tongue, pharynx and larynx, the cervix uteri, the vulva and penis, anus, some cancers of the breast and rectum and certain bone sarcomata.

The " beam " can be employed to cure or to palliate growths of the hypopharynx, pyriform fossa, tonsil and pharyngeal wall which formerly were quite hopeless or amenable only to operative measures which were dangerous, mutilating and frequently ineffective. It must not be forgotten, however, that even by this new method violent reactions may ensue, and that the patient may suffer extreme discomfort and dryness of the mouth and dysphagia. Therefore it should not be employed unless the growth is of a reasonable size, or alternatively, in the more advanced cases, the dosage should be reduced.

Speaking generally, effective as gamma-ray treatment may be for primary growths, it is seldom possible to prevent glandular deposits by the methods at present in vogue. It is, I think, probable that the results of massive radiation from a 5-gramme bomb, when this information eventually is available, may cause us to change our outlook on this matter. In the meantime, the trend of opinion is in favour of a

systematic block-dissection of glandular drainage areas whenever these are accessible and the condition of the patient justifies it. My own experience so far is emphatically that glandular metastases are the province of the operating surgeon, and that the wider and more systematic the extirpation of these glands the better the eventual result.

While we must rate radium therapy very high in the treatment of certain cancers, as I have already admitted, the difficulties, dangers and inconveniences of the method are now only too well known. If it were certain that the radiation from radium is alone of real value in cancer therapy, there would be little justification for seeking substitutes for it, but there is abundant evidence that radiation of longer wave-lengths than the gamma-rays is of considerable efficacy in destroying cancer cells; in fact, the optimum wave-length for every type of growth is not known. It is, however, believed, and with some justification, that the shorter waves are of greater efficacy than the longer, and that the nearer they approach in quality the gamma-rays from radium the more valuable therapeutically.

For this reason attempts have been made recently to develop X-ray therapy, utilizing higher and higher voltages so that harder and harder rays are produced. Assuming a biologically similar effect, the advantages of deep X-ray therapy over radium therapy are that an apparatus costing about £3,000 can be made to do the work of 170 grammes costing about £3,000,000 without any extra expense in the way of running costs. At the Cancer Hospital we have been working with a voltage approximating to 400 k.v. At the Memorial Hospital, New York, 700 k.v. have been used for about three years, and there seems to be no reason why eventually the voltage should not be raised sufficiently to bridge almost entirely the gap which still exists between

gamma-rays and the hardest X-rays yet utilized in cancer treatment. Already the results obtained by the higher voltages have shown a great advance on those gained by the usual 180—220 k.v. apparatus, not only when used as a substitute for gamma radiation, but also when they are employed in conjunction. I can foresee the time when deep X-ray therapy will to a large extent, if not wholly, replace radium therapy, but I am not sufficient of a prophet to foretell how soon this will come about. At the Memorial Hospital, New York, careful comparisons have been made between the physical, biological and therapeutic effects of the X-rays of 200 k.v., 700 k.v. and gamma-rays from radium (G. Failla McNalton et alii, 1933).[59] It is impossible to summarize their results satisfactorily, but in respect to cancer of larynx, pharynx, hypopharynx and tonsil (which are accessible and easily observed sites), working with divided doses and 700 k.v., it was found that the local and general discomfort were both reduced as compared with what happens with 200 k.v. and with gamma-rays from radium. It is not possible at present to say whether this conclusion can be expanded into a generalization applicable to other types of growths at various sites. Much in this connexion is to be expected from the adoption of the universal *r*-unit for X-ray dosage, as this will enable much more reliable comparisons to be made between these therapeutic measures.

It has been shown that deep X-ray therapy, combined with gamma-ray therapy, is capable of giving a higher percentage of cures or a more complete palliation in the treatment of cancer at certain sites, *e.g.* carcinoma of cervix, than is gamma-ray therapy alone. As an adjunct to surgical measures there can be no doubt whatever from my own experience and that of others that deep X-ray therapy, especially from high voltage apparatus, is essential if the best results are to be arrived at. I have some evidence that in acute cancer of the breast in young or lactating women deep X-ray therapy will render what appeared an inoperable case operable, while after operation it can be applied far more effectively against recurrence than any form of gamma radiation, except, perhaps, the "beam" from a 4- or 5-gramme unit. Dawson and Tod[60] (1933) recently collected some reliable figures in relation to carcinoma of the breast which show that the combination

of operative methods with post-operative X-ray therapy increases the five-year survival rate by nearly 10 per cent. Comparable figures could be quoted, I believe, in relation to cancer of the tongue, lips, floor of mouth, palate, pharynx, etc., in all of which, even after the disappearance of the primary lesion following gamma radiation and the most radical block dissection of the cervical glands, deep X-ray therapy is needed to destroy outlying cancer cells in the remoter lymphatics, and especially in the zone of tissue between the original growth and the area embraced by the block dissection.

Chemotherapy.

Ehrlich's successful attack on the Treponema has stimulated the search for some compound which should destroy the cancer cell and prove as effective as does salvarsan in the control of syphilis. Unfortunately, the theoretical basis for such a research is less sound than was Ehrlich's, since there is so little evidence of any physico-chemical differences between the normal and the cancer cell, though it is true that Warburg[61] has described powerful glycolytic powers for some cancer cells. This property is not, however, specific to cancer cells, being exhibited also by the retinal cells and by those of the placenta.

It is possible that the various chemical substances which have been tried in cancer therapy act—

(1) Directly, *i.e.* on the cancer cell itself; or

(2) Indirectly, by increasing the power of the body cells to resist the growth of the cancer cell.

Caspari,[62] for example, conceived that the metallic salts he employed became precipitated in the tumour and increased autolysis, with the formation of necro-hormones, which, carried into the blood-stream, stimulated the reticulo-endothelial cell system. Wassermann believed that tumour cells have an affinity

for certain chemical compounds (*e.g.* eosin), and that this could be utilized to carry selenium to the tumour. Ludford's[63] experiments on dyes suggest that they are deposited, not in actively growing cancer cells, but in those which are degenerating, and that the bulk of the deposit is in the connective tissue in and around the tumour masses—especially the primary. The Golgi apparatus appears to play an important part in the segregation and elimination of the dyes.

Successful chemotherapy demands (1) an intravenous administration, in order that all secondary deposits may be affected as well as the primary lesion; (2) the agent should be deposited chiefly in the tumour cells and the connective tissue in the neighbourhood, a condition which Kawata's experiments render very unlikely, since in cancerous mice treated with lead the latter is found mainly in the liver and very little in or near the cancer cells; (3) the ratio of the toxicity of the compound for body and for tumour cells respectively should not be less than 1 : 3—an almost insuperable difficulty.

With the object of finding such an ideal form of chemotherapy numerous metallic and other compounds have been tested. With Wassermann's original selenium injection the survival rate was only 3—5 per cent. owing to the toxicity of the drug.

Neuberg and Caspari[64] employed copper, selenium, tin, zinc, cobalt and silver sometimes in colloid form, but while necrobiotic changes were observed in the tumours, the mortality was prohibitive. Curiously enough, in view of Todd's work, they noted a stimulating effect in the tumours with small doses of the various colloidal metals. Keysser systematically re-investigated the action of selenium in 1914 in animals, and could find no evidence that it has any action if the tumour is small, though it may produce shrinkage in already degenerating neoplasms.

Clinically Touche in 1913,[65] reported good results with selenium therapy, more especially as a palliative method.

Blair Bell[66] in 1922 observed benefit from the use of approximately 0·5 gramme to 0·8 gramme of lead in a concentration of 0·5 per cent. The preparation he employed was alleged to be a colloidal one, obtained by the Bredig process. The method of administration was modified from time to time after it was first introduced, chiefly by spreading the injections over a more extended period than at first.

Some cures were claimed, in addition to a considerable percentage of cases of arrest of the disease, and many in which the pain had been alleviated. In some of the cases radiotherapy and surgical extirpation were employed in addition to lead therapy. Many independent observers, including Hume,[67] Wyard,[68] Burton Simpson[69] and Thomson,[70] have failed to obtain such favourable results, and the majority of these authors report a high morbidity and prohibitive mortality. I can myself testify that at the Cancer Hospital lead treatment was given a most careful and exhaustive trial, and that the results were deplorable. Todd's colloidal lead selenide is much less toxic than Blair Bell's preparation, and appears to be as successful. It is very interesting, and perhaps significant, to note that lead therapy has apparently been entirely abandoned in Liverpool, where it was initiated and actively persisted in for so long a period.

Copeman, Coke and Gouldesbrough[71] have sought to enhance the effect of X-rays by adding a fluorescing substance which they assume produces a secondary radiation in the neighbourhood of the tumour cells, thus adding to the lethal effect of the primary radiation. They inject 20 cc. of 5 per

cent. Sodium Fluorescine intravenously or paint it on to the surface of superficial tumours.

Dr. Todd's[72] recent work in cancer-therapy constitutes one of the most earnest and thoroughly systematic attempts to treat inoperable or otherwise apparently incurable growths. The following is an outline of the method as practised at present, though perhaps it is supererogatory for me to describe it to a Bristol audience.

Dr. Todd believes that such beneficial effects as X-rays and gamma-rays may have in the treatment of malignant disease are the result of their action on the connective tissue in and about the neoplasm itself, this tissue being regarded as inhibitory to neoplastic growth and termed "junction" tissue. His experience in human beings and his experiments in mice lead him to the conclusion that X-rays and gamma-rays applied in the usual dosage on subjects impregnated with selenium colloids may actually stimulate the growth of the cancer, and he explains this as due to a destructive or paralytic action on the "junction" tissue.

Acting on this hypothesis, Todd has abandoned the use of lead selenide (D4S) in conjunction with massive radiation, and has substituted for it a sulphur-selenium colloid containing no metal, combining this with X-radiation. The colloid is administered intravenously once weekly, or fortnightly in specially sensitive cases, and forty-eight hours later the dose of X-rays is applied. Todd concludes that the particles of selenium are acted upon in the "junction" tissue by the penetrative radiation, the effect being termed ionization, and the result held to be a stimulation of the junction tissue to check neoplastic growth.

Experiments are being carried out in his laboratories to show whether short wireless waves, approximately of two metres wave-length, will induce this ionization effect, and for some time he has employed a selenium colloid therapeutically which is radio-active in order to induce a state of permanent ionization in the "junction" tissue.

Dr. Todd claims :—

1. About 50 per cent. "3-year apparent cures" of inoperable cancer of the breast and of the ovary.

2. About 60 per cent. "3-year apparent cures" in sarcoma generally.

Speaking as one who has had the opportunity of studying malignant disease in its inoperable forms from beginning to end in the chronic wards of the Cancer Hospital, I am obliged to offer certain criticisms of Todd's views. It is by no means rare for cancerous masses, both primary and secondary, to diminish in size, ulcerating growths may heal up wholly or partially, and patients may improve in health and increase in weight even when no specific attempt is made to treat the neoplasm. So far as I am concerned I have never known a single case of idiopathic regression or apparent arrest of tumour growth in which eventually recurrence did not manifest itself, but sometimes the quiescent interval is prolonged.

It is only fair to state, too, that there are records —some highly circumstantial—of nearly 400 cases of complete spontaneous cure of cancer.

I can, however, testify to the optimistic outlook of the patients under Dr. Todd's care and to the subjective improvement which many of them report.

My main ground for criticism is that there is no evidence that effective ionization (or secondary radiation) occurs with the doses of selenium which are employed. Mayneord and Burrows'[73] work indicates that it would require a dose of the selenium colloid several hundred times as great as that administered by Todd to produce the minimal effective ionization, even allowing for a high selective concentration of the colloid in and around the tumour cells and stroma. Finally, the method of checking the progress of treatment by Rona's serum-lipase estimation has been clearly demonstrated to be quite fallacious.

Serum Therapy.

The last therapeutic method to which I need refer is that of Lumsden. Here we are dealing with an attempt to provide a universal cure for cancer—chimerical, if we accept the main thesis of my lecture—but one extremely attractive to many cancer-therapeuticians and to all laymen.

Lumsden[74] is endeavouring to prepare a serum which will stimulate the natural powers of resistance of the normal tissues to the spread of cancer cells. He claims that antibodies of this nature occur in the blood-serum, and that the reticulo-endothelial cells produce a cytase which damages the malignant cells and they then become the prey of the antibodies. He has obtained sera which will destroy cancer cells in animals, but the amount of antibody is so small that unless it can be concentrated it is ineffective in man. In animals the concentration of the antibody is effected by shutting off the circulation to the tumour temporarily. It is claimed by Lumsden that by fractioning off the euglobulin of the serum the concentration of the antibodies which adhere to the euglobulin is thereby increased tenfold. This concentrated serum is now being employed in treating inoperable cases of cancer at the London Hospital, but the introducer of the method admits that much research is still necessary, and that many years may elapse before the method is perfected.

Mr. Vice-Chancellor, in concluding this lecture, and in thanking my hearers for their courteous attention, may I be allowed to stray beyond the limits imposed by my own choice of title? Only a few days ago I returned from an International Conference on Cancer, and there I could not help being exalted by the optimism of the younger school, both research workers and clinicians, and depressed by the slightly cynical pessimism of the older school. I believe that the young men are right, that with the aid of vision and

courage the causes of cancer will be discovered, and that such knowledge will inevitably lead to the formulation of methods, not so much of cure, as of prevention. The essential clues to the cancer mystery lie in the biochemistry of the cell, and in the amazing powers of the hormones of the various endocrine glands, which are only now beginning to be realized, but I am confident that with the broadening of our knowledge of these subjects will come the clarification of the whole cancer problem.

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THE PRESENT POSITION OF RADIUM THERAPY.*

BY

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RADIUM has been described (I have forgotten by whom,) as the most potent element which has been yet discovered for the production of discontent in the medical profession. It was hailed at first as a panacea for all ills. Although it has not fulfilled the hopes based upon it by those early enthusiasts, it has opened up new fields in the treatment of disease, especially malignant disease, but even there, despite improved technique, I do not think that radium is at present a substitute for surgery. The radium needle should be looked upon, not as a competitor to the knife, but as a partner and an added weapon in the fight against cancer.

Radium therapy should be restricted to inoperable cases or those cases where operation is attended by great risk, such as Wertheim's hysterectomy, or associated with mutilation, such as removal of the tongue. Of the inoperable cases those that are very far advanced with widespread metastasis, bony

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involvement, much sepsis and marked wasting are generally unsuitable; while patients suffering from diabetes, nephritis, syphilis or tuberculosis do not, as a rule, respond well to radium treatment. In addition, accessibility of the lesion, its proximity to vital structures and its histological type modify the results. Adeno-carcinomata are considered radio-resistant and well-differentiated squamous-celled carcinoma less resistant, while non-differentiated epithelioma and the basal-celled carcinoma or rodent ulcer are radio-sensitive. Many of the sarcomata, especially lympho-sarcoma, are extremely radio-sensitive, but unfortunately these growths tend to recur either locally or elsewhere very soon after irradiation.

Roughly about 50 per cent. of the malignant cases treated by radium are locally well, mostly symptom-free at the end of one year. This is a considerable achievement, as the majority of these cases are hopeless from a surgical point of view, and so, were it not for radium treatment, most of them would have been dead and certainly none of them would have been symptom-free at the end of a year. There is, as William Mayo says, a great difficulty in evaluating radium treatment, since it is used so largely in treating inoperable cancer or cancer following operation, where the most that can be expected is palliation. The thoughtless, therefore, give radium little credit for what it actually accomplishes in these cases and, disappointed that the impossible has not been accomplished, minimize its value. I mention one year as the period of freedom from symptoms, not because I believe that recurrences either occur within one year or not at all, but because the patient and

his doctor are more interested in the immediate effects of radium treatment and are less concerned with what will happen five years hence; and secondly, techniques have altered so rapidly within the last few years that reliable five-year statistics are difficult to obtain.

At the outset I should like to make it clear that the results mentioned in this paper are the average results obtained from a number of centres. Gordon-Watson, I know, has obtained good results in carcinoma of the rectum, and Geoffrey Keynes's results in carcinoma of the breast are excellent; but these are exceptional, and at the majority of centres results are less promising when these regions are treated.

In spite of advances in the knowledge of the biological and physical properties of radium, the conditions governing the vulnerability of normal and malignant cells are still, to a large extent, problematical, and we still do not know why two apparently similar cancers with apparently similar histological structure will react in a dissimilar manner to radium. The histologist and cytologist have worked long and hard at the problem, and the solution, I think, now lies in the hands of the bio-chemist and bio-physicist. However, just as the majority of practitioners do not consciously think of the exact *modus operandi* of the drugs they use, we radiologists use radium even if the processes initiated in the tissues by radiation are far from being understood.

There are four main radium techniques. The *first* is that of interstitial needling, in which radium is inserted surgically into the diseased tissues. This

method is that most often employed at present, but requires a general anæsthetic; the lesion is surrounded by needles which are left in place for six to fourteen days, depending on the histological type of lesion, the strength and filtration of the needles. *The second method*, the intracavitary method, is that in which radium is placed in a natural cavity of the body, for example, in the body of the uterus or in the œsophagus. This treatment rarely lasts for longer than a week. *The third method*, that of surface treatment, consists of covering the surface of the lesion with radium, which may be directly applied to it or separated from it by ¼ to 4 cm. of some material such as wax or rubber. Treatment here may last from a few hours up till ten to fourteen days, depending not only on the type of lesion and the concentration of the radium, but also on the distance of the lesion from the radium. A small superficial lesion will, of course, have the radium closely applied to it. *The fourth method* of treatment is the much discussed distance radium or mass irradiation therapy, when a bomb containing a large quantity of radium is placed at some inches from the body. There are many conscientious enthusiasts who advocate the use of the bomb: equally many decry it. Results on the Continent have, on the whole, been good. The lack of success in England may, perhaps, have been due to our lack of proficiency with smaller units, but it seems to me that before we can use huge quantities, such as 15 grammes, we will want not only larger hospitals to house the radium, but bigger and stronger patients to stand the treatment. There is no definite therapeutic difference between the use of element

radium and its emanation radon, except that radon, being a gas, can be collected, compressed and sealed in small containers known as seeds.

Shortly after the beginning of radium treatment the lesion becomes covered with a smooth, greenish-yellow fibrinous exudate not unlike a diphtheritic membrane, which increases for about three weeks, when it gradually fades away from the edge, being replaced by healthy tissue. When radium is applied to the unbroken skin, *e.g.* in the treatment of a deep-seated mass, this reaction is preceded by reddening of the skin and desquamation. This typical reaction is not a burn, although when it appears on what was formerly unbroken skin the uninitiated may refer to it as a burn. Sometimes, however, the reaction may last longer, and in the case of over-dosage may persist for months with the formation of an ulcer. The radio-necrotic ulcer or burn has usually a sharp, punched-out edge instead of the smooth edge of the normal reaction. It occurs at the centre of the site treated, may be deep, and is often very painful. The best treatment is removal by diathermy. The presence of a radio-necrosis is not always due to bad technique, any trauma, intense heat or cold, etc., may cause it, and it may occasionally be due to a personal idiosyncrasy on the part of the patient.

Lesions of the *Skin* may be treated by either surface or interstitial radium. Results on the whole are equally good. These lesions are usually radio-sensitive, and, provided bone is not involved, good and lasting results may be expected in the majority of cases. Radium therapy here is definitely superior to surgery, since there is no mutilation, the lesion

being replaced by a supple scar. Should glandular metastasis arise in association with a lesion in any part of the body it should be dealt with surgically. Epitheliomata on old lupus do not give such good results, as a great number of them recur after a year. Sometimes it is worth while treating this recurrence, but as the skin is very devitalized, another occurs rapidly, or necrosis appears. In rodent ulcer the results are excellent and superior to any other form of treatment.

Lesions of the *Lip* may also be treated by either surface or interstitial treatment. The results here are very good, and up to three-quarters of even the most advanced cases may be alive at the end of the year.

The opinion of most gynæcologists is that radium is preferable to surgery in carcinoma of the *Cervix Uteri*, since there is very little risk and even the most advanced cases derive benefit. As a rule bleeding and discharge become appreciably less and frequently cease, and about half of the cases treated are alive at the end of the year. Sometimes an apparently cured case complains of backache. This may be due to involvement of the ureters in fibrous tissue, a condition which the gynæcologist can sometimes relieve. Treatment usually consists of intra-uterine and vaginal applications for about seven days, either continuously or in separate applications spread out over three to six weeks. Sometimes interstitial needling is used. Post-radium X-ray therapy has increased the number of good results. Unfortunately, results of radium treatment are disappointing in this region if the patient is under forty, and if the case

is operable it is advisable to operate. Opinions differ on the value of radium therapy in carcinoma of the *Body of the Uterus*. Some centres report results equal to those obtained by surgery, but I think the majority of centres regard adeno-carcinoma of the body of the uterus as being radio-resistant. In carcinoma of the *Vulva* radium therapy gives bad results. Temporary disappearance of the growth is frequently obtained, but, possibly due to interference with the blood supply, the dose sufficient to kill the growth usually causes a necrosis of the tissues with the formation of a deep, sloughing, painful ulcer.

In carcinoma of the *Mouth, Tongue and Tonsil* results are encouraging, as, with a negligible primary mortality, about half of the cases are alive at the end of the year. If, however, there is bony involvement radium treatment may result in a slow and painful necrosis. When the tongue is absolutely fixed, palliation and some relief from pain is sometimes obtained by applying very large doses of radium for a short length of time. In extremely advanced cases radium is, I think, contra-indicated, as a certain amount of œdema and pain follow treatment, and so, for no useful purpose, the patient's discomfort is aggravated. The majority of lesions on the inside of the *Cheek* seem to arise from an old leukoplakia, and so the results here are disappointing, and less than 50 per cent. are said to be symptom free at the end of one year. Treatment usually consists of interstitial needling, but occasionally surface applicators are used. The latter are said to give better results.

Carcinoma of the *Anus*, being a squamous-celled

carcinoma, responds well to radium, and even in very advanced cases treatment may produce temporary and local relief. Carcinoma of the *Rectum*, however, being an adeno-carcinoma, gives on the whole bad results, although occasionally after radium an inoperable case becomes operable. In this site radium may be inserted interstitially into the growth or a central radium applicator may be passed into the rectum, but the latter method is not frequently used nowadays.

The radium treatment of carcinoma of the *Bladder* is still more or less in an experimental stage, but some good results have been reported from the New York Memorial Hospital. Because of their small size radon seeds are more suitable than needles. The usual method of treatment consists of opening the bladder and inserting the radium into the base of the growth, where it remains for about eight days, or, in the case of seeds, for ever.

The value of radium treatment of carcinoma of the *Prostate* is still on trial, and no figures are available from any of the larger centres, although quite good results have been reported by individual surgeons. Needles are usually inserted interstitially through the perineum or bladder.

In the treatment of carcinoma of the *Breast* radium has not realized our earlier hopes, and operation is still the method of choice, perhaps combined with radium. In inoperable cases, or those showing one or two bony nodules, radium (either used in the form of a surface application or interstitially) sometimes produces temporary palliation with disappearance of the mass, but very advanced cases with marked skin or glandular involvement derive no benefit.

Intrinsic carcinoma of the *Larynx* gives very good results when combined with fenestration operation, and palliation has been obtained in some extrinsic carcinomata.

The results from radium treatment of carcinoma of the *Antrum* are gradually improving, due perhaps to a closer co-operation between the radiologist and the surgeon. Treatment consists, as a rule, of opening the antrum and the distribution of needles or seeds around the growth. This may be followed by a surface application on the outside of the face.

Carcinomata of the *Internal Organs* and of the *Alimentary Tract* respond badly to radium. In carcinoma of the œsophagus disappearance of the growth has sometimes occurred, but it recurs in about six months, and similar benefit may be obtained by the insertion of a Souttar's tube without the use of radium.

It is not only in malignant disease that radium has proved of benefit. Indeed, if it had no other field of usefulness except its ability to control uterine hæmorrhage, it would be a remarkable therapeutic agent on that basis alone. But, in addition to these uses, it has proved of benefit in many skin lesions such as tuberculous ulcers, warts and corns, and is at present being tried out, with some measure of success, in other conditions, such as painful bursas, goitres, etc.

In writing this paper I have kept in front of me the advice of Pasteur: "Your enthusiasm, which is the fruit of your earlier years, keep it, but let it be attended by a rigorous self-control"; and I have tried to show you the real worth of

radium by being neither unduly optimistic nor unduly pessimistic.

Whatever may be the ultimate place that radium will gain and hold in the armoury of the surgeon and the radiologist, it has already certainly proved to be a most useful palliative agent and has a definite curative value in a good many cases.

BACILLUS COLI INFECTIONS OF THE FEMALE URINARY TRACT.*

BY

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VULVO-VAGINITIS.

PRIMARY infection of the vulva, vagina and urethra with B. Coli is not common, but cases do occur which give rise to a suspicion of gonococcal infection. The commonest type is the vulvo-vaginitis of young girls; this is limited to the external genitals, and does not involve the vagina above the hymen and rarely the urethra. The initial lesion is usually caused by trauma, either by the rubbing of tight-fitting underclothes or by scratching from irritation, usually due to thread-worms, and infection by the B. Coli follows. On the other hand, excoriation of the parts may be caused by a highly acid urine, with subsequent Coli infection. The labia are swollen and red, and there is thick tenacious pus between the labia majora, which may be glued together. The pus is limited to the external genitals, and none can be expressed from the vagina by pressure made by a finger in the rectum, whereas in gonorrhœal cases pus can usually be expressed in this manner. The urethra is rarely

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infected, whereas in gonorrhœal cases it is almost invariably so. Differential diagnosis, however, rests mainly on bacteriological examination, which shows in the non-gonococcal variety a predominant growth of B. Coli, with some staphylococci.

These cases rapidly clear up under treatment, which consists in keeping the parts clean and bathing them with a weak antiseptic lotion. I have found potassium permanganate as efficacious as any, even in the non-gonorrhœal cases. After this the parts are dried with a soft towel by "dabbing," not rubbing, and then an antiseptic dusting powder is applied. If the labia tend to adhere, then an ointment may be applied between them, or lint covered with ointment placed in the natal cleft: this is especially useful at night. The initial cause must be dealt with, such as large doses of alkalis for acid urine, the treatment of the thread-worms, and the abandonment of the tight-fitting underclothes. The irritation is usually worse at night, and if this is the case then gloves should be worn by the child.

Vulvo-vaginitis of Coli origin is sometimes met with in newly-married women, and again suspicion of a gonococcal origin arises. The symptoms, however, are mild; bacteriological examination shows the presence of B. Coli in almost pure culture, and the absence of gonococci. The condition rapidly clears up under the treatment already outlined, and this rapidity of cure almost proves the non-gonorrhœal origin of the lesion.

CYSTITIS.

Cases of acute and chronic cystitis are frequently met with in the gynæcological out-patient department, either alone or associated with pyelitis.

Large numbers of B. Coli can be passed through the bladder without setting up a cystitis, and therefore one is bound to presume a second factor as necessary to produce this condition. This factor is some local lesion of the bladder, which may be trauma or the lowering of local resistance by "chill." Trauma is the most usual cause as in catheterisation, or operation such as stripping the bladder down in performing a panhysterectomy, or again it may be due to the presence of residual urine as in the sacculated bladder of prolapse, or retention of urine caused by a pelvic tumour or the retroverted gravid uterus. Coli infection of the bladder is common after gynæcological operations, and I am sure that this is largely due to rough handling of the bladder. The infection in these cases is limited to the bladder, and does not ascend to the kidneys. The infection in B. Coli cystitis may be an ascending or a descending one; the ascending infection, in my opinion, is the most common, and I doubt whether a descending infection occurs except as an extension from a pyelitis. I do not think that a bacilluria can exist without some lesion of the urinary tract, and that the disease B. Coli bacilluria is non-existent: that it is a symptom and not a disease. I consider the presence of a large number of B. Coli in a catheter specimen as showing a lesion somewhere in the urinary tract.

Ascending infection in the female is simple: the source of infection is the anus, there is no protective bacterial flora in the urethra as in the vagina, and the urethra in the female is constantly exposed to infection; it is easily entered, is short and capacious, and it only requires some local lowering of resistance or trauma and a cystitis is set up.

In the B. Coli infection of young girls no local

lesion is demonstrable, and it is probably due to the lowering of resistance by exposure to cold. The constitutional symptoms in some cases are so severe as to suggest a bacillæmia, and this view has been put forward as the origin of all Coli infections of the urinary tract. This I want to discuss later when dealing with pyelitis.

Acute Cystitis.

In the acute cases the symptoms complained of are frequency of micturition, both day and night, pain on passing urine, which pain is usually referred to the urethra, and is burning or scalding in character. There is a constant dull pain in the hypogastrium, often described as "dragging," and this is worse after emptying the bladder. The pain of a pure B. Coli infection, however, rarely reaches that acuteness found with other infections, and strangury is not common.

The temperature is raised, but it is never as high as in infections of the upper urinary tract, the pulse-rate is rarely increased. On examination there is tenderness over the hypogastrium, which is very marked on bimanual examination by pressing the anterior vaginal wall up against the abdominal fingers. The mouth of the urethra may be pouting and œdematous, and the vulva and inner sides of the thighs excoriated.

The amount of urine passed is copious, and if examined by the naked eye in a specimen glass there is a definite glistening sheen, very little debris, and this chiefly mucus. The reaction is highly acid: an alkaline reaction means a mixed infection, and then pus in the specimen glass is abundant. On microscopical examination B. Coli are found in abundance, a

few pus-cells, bladder epithelium and a few red blood-cells. On cystoscopic examination there is swelling of the mucosa, and a certain amount of ropy mucus adherent. There is rarely ulceration except over a damaged area, which is usually at the base.

Chronic Cystitis.

Chronic B. Coli cystitis is rare apart from cases accompanying chronic pyelonephritis, and these are common and will be discussed later. Chronic cystitis occurs where there is some obstruction to the outflow of urine from the bladder. The most common example of this is in cases of cystocele, where, owing to the base of the bladder being below the urethral opening and the musculature stretched in this region, the bladder is not completely emptied at each act of micturition. The result is a certain amount of residual urine, which soon becomes infected via the urethra. Frequency, pain on micturition, and a sense of fullness in the hypogastrium are the symptoms which bring a large number of patients suffering from prolapse to the doctor, and very little good is done by treating the cystitis without treating the prolapse. Relief of symptoms may be obtained, but a series of relapses is inevitable.

Another frequent cause is a pelvic tumour either adherent to the bladder, dragging on it and causing sacculation, or pressing on the urethra or base of the bladder. In the last case, however, there is usually a preliminary attack of acute cystitis, and the case can only be labelled chronic in that there are a series of relapses of a less severe nature than the first.

Physical signs are few, there is no marked

tenderness of the bladder, but the urethral orifice is usually pouting and red, and there may be excoriation of vulva and thighs. The underlying cause of the cystitis, usually prolapse, will, however, be found. In elderly patients these signs and symptoms may be caused by glycosuria, and the urine should always be tested for the presence of sugar. A number of cases of glycosuria have been treated for long periods under the mistaken diagnosis of chronic cystitis and vulvitis.

On cystoscopic examination the bladder mucosa is thickened and covered with mucus, there is rarely any marked contraction, but in prolonged cases, and especially in elderly women, there is atrophy of the mucosa, but rarely sacculation, though the capacity of the bladder may be considerably diminished. This is usually due, however, to a senile change rather than to an inflammatory fibrosis.

The symptoms of chronic cystitis are very slight, viz. frequency of micturition and a feeling of fullness in the hypogastrium; there is rarely pain on micturition and no constitutional disturbance. The urine examination shows much the same contents as in acute cystitis, but the bacteria are fewer in number, an occasional pus-cell, large numbers of bladder epithelial cells and very rarely a red blood corpuscle. In those cases accompanying a chronic Coli pyelonephritis the ureteric orifice on one or both sides is pouting and surrounded by a hyperæmic area of the mucosa. The treatment of acute and chronic cystitis we will discuss under that of pyelonephritis, as these two conditions demand almost identical therapy, though the latter requires more elaboration.

PYELONEPHRITIS.

This is a very common disease of the female; it is much more frequently met with as a complication of pregnancy than in the non-pregnant state. It is a not infrequent complication of the puerperium and of gynæcological operations, though it does occur often apart from these conditions. The spread of the infection in the female is almost always a descending one; ascending infection is rare, except in cases of pelvic growths invading or obstructing the outflow of urine from the bladder, and then is a mixed infection.

The source of the B. Coli is almost certainly the bowel, but views differ as to the route taken to reach the kidney. The older view was that the infection was hæmatogenous in origin and that the primary condition was a bacillæmia, that in health the kidneys were capable of excreting the bacteria without damage to the kidney substance, but if the invasion was overwhelming, or that there was some local condition of damage or obstruction to pelvis or ureter, then pyelonephritis arises. Against this we have the considerations that B. Coli has rarely been cultured from the blood in these cases, that no other organ or structure in the body is attacked, and that the infection is most frequently unilateral, whereas with a generalized infection one would expect a bilateral infection in all cases. The only fact that can be advanced for hæmatogenous origin is the occurrence of rigors and the swinging temperature of the disease, but these only commence with the onset of local kidney signs and symptoms, whereas in a bacillæmia these should be present before the local signs.

The most likely route for the infection is by the lymphatics: either a direct infection from the bowels

or from the bladder via the ureteric lymphatics. The last method is not compatible with the clinical picture, as the chief and primary lesion falls upon the pelvis of the kidney, and the bladder is only infected secondarily.

Direct infection from the bowel is simple. On the right side the lymphatics of the cæcum are in direct communication with those of the pelvis of the kidney, while those on the left are more indirectly connected with those of the descending colon. This accounts to a large extent for the greater frequency of right-sided infection.

Pathologically, the whole kidney is involved in the lesion, though clinically we speak of a pyelitis. The main lesion falls on the pelvis of the kidney, the mucosa of which is swollen and covered with muco-pus. The kidney substance shows various degrees of invasion; in the mild cases the organ is enlarged, tense and deeply congested, while in the more severe cases multiple small abscesses may be found. The pelvis of the kidney may be dilated and the ureter blocked with inspissated pus and debris, giving rise later to a hydronephrosis. The dilatation of the pelvis, however, is most marked in cases of pyelo-nephritis of pregnancy, and it is to this condition that I want to draw your especial attention. Dugald Baird, of Glasgow, in the Bradshaw Lecture to the Royal College of Physicians last year, brought the pathology and pathogeny of this subject up to date and added much to our present knowledge of this condition. Since then I have hoped for an opportunity to confirm his findings, as I believed them to be correct. Early in the year I had a case of pyelo-nephritis of pregnancy, which pregnancy I found necessary to terminate by evacuating the uterus at

the sixth month of pregnancy. I evacuated the uterus by hysterotomy, and afterwards made a detailed examination of the urinary tract on both sides and fully confirmed Baird's findings. This case I will describe in more detail later.

It will thus appear that the first factor in the production of acute pyelonephritis is a descending infection via the lymphatics to the kidney from the bowel. In the pregnancy and the enlarging uterus we have the second necessary factor. Greenine and various workers have shown that in pregnancy there is always atony of the upper urinary tract, commencing early in pregnancy, probably due to some endocrine deficiency, and this is thought by Baird to be deficient posterior pituitary secretion. This atony affects both of the ureters and pelves equally; it also causes the ureters to be easily compressible, and the compressing agent is the uterus, and the site of compression the pelvic brim. The greater frequency of right-sided lesion was said to be due to the uterus being more frequently twisted to this side, but observations made at Caesarean section have shown that this is not the case; it may not be twisted at all, and is nearly as often twisted to the left as to the right, and when twisted to the left there has been no corresponding dilatation of the left ureter. Baird has advanced the hypothesis that the greater frequency on the right side is due to the more exposed position of the ureter as it crosses the common iliac artery, while on the left it passes parallel with the vessels and is protected by them, and also passes under the sigmoid, which again protects it. Whatever the cause may be, the right ureter is definitely compressed at the pelvic brim, and this was shown beautifully in my case. Above the brim the ureter was the thickness of a finger all

the way up to the pelvis of the kidney, and showed up as a ridge beneath the posterior peritoneum, while below it was only palpable. There was some thickening of the left ureter, but not nearly so marked as the right, and there was no demarcation at the pelvic brim. Baird has described kinks, especially at the junction of the upper and middle thirds; these were not present in my case. Such kinks may represent a more advanced stage of the lesion, which is most probable, as his specimens were obtained at autopsy. By pyelography he has shown dilatation of the pelvis and calyces of the kidney, whilst estimation of kidney function has shown definite impairment. On passing a ureteric catheter in the aforementioned case of mine, at the time, a small amount of urine, pus and debris were evacuated, but later there was no drainage from this kidney at all, and on palpating the kidney at operation it felt firmer and smaller than that on the left side. I wondered if owing to the prolonged back-pressure it had ceased to function, but this is hardly likely, as the pressure of the uterus could never cause complete obstruction of the ureter; but this small fibrotic kidney does correspond to some of the post-mortem kidneys found in the condition. I cannot do better than sum up these pathological conditions in Baird's own words:—

"The usual sequence of events in pregnancy is as follows. At the beginning of pregnancy a primary atony of the ureters occurs. In some this is very slight and may be scarcely appreciable. In others it affects both ureters, equally in primigravidæ, but in multiparæ it may be more pronounced on one side, usually the right, where presumably there has been a previous dilatation of a marked degree. At the third month the primary atony disappears. At the

fourth to the fifth month delay in excretion occurs, usually more marked on the right side. At this stage the delay may be due to atony without dilatation; but, more commonly, dilatation of the ureter above the pelvic brim can be demonstrated. The degree of stasis is not in proportion to the amount of dilatation present, as considerable dilatation may be present without any stasis. In some cases spasm of the ureter at the pelvic brim can be demonstrated at this stage, causing severe spasmodic pain over McBurney's point. In such cases there is marked activity of the urinary tract, but delay in excretion occurs due to the spasm, and there is dilatation and kinking of the ureter above the site of the spasm. Where dilatation is accompanied by atony pain is usually absent, but if present is slight and of a dull aching character. The spasm of the ureter is probably the result of the pressure of the uterus, as it can be produced by an ovarian tumour of the same size. The stasis and dilatation become more pronounced until they reach a maximum, usually at the sixth month. From then until term elimination slowly improves. On the left side, where the delay usually has been less marked, this improvement, which may be accompanied by a decrease in the amount of dilatation, is easily seen; but on the right side, when there has been very marked stasis and dilatation, there are technical difficulties in the way of appreciating moderate degrees of improvement. Within a very short time after delivery the ureters again show atony, although the excretion time may be improved."

Clinically the disease may be divided into two types, severe and mild.

In the severe type the onset is sudden, often with an initial rigor, and these may be repeated during the

course of the disease. In pregnant cases the onset is usually about the fifth or sixth month of pregnancy. The temperature is high, temperatures of 105° F. are common; on the other hand, the pulse is not unduly rapid and does not correspond to the temperature; later in the disease, however, it may become rapid, and is then a disquieting feature. Pain is referred to one or other loin and the lower abdomen, and there may be some rigidity, and right-sided infection is sometimes mistaken for appendicitis. The pain may be paroxysmal in character, and is then referred to the lower abdomen, but usually the pain is fixed and referred to the loin. There is frequency and pain on micturition, and paroxysmal pain may be associated with this.

On examination there is tenderness over the affected kidney and palpation is resisted, but when the kidney can be felt it is usually enlarged and tender. The urine is highly acid, pale in colour, and a deposit of white muco-pus forms on standing, but this is not always the case, the urine may be quite clear owing to blocking of the affected ureter.

Microscopical examination shows the presence of pus, epithelial and granular casts, a few red blood-cells and B. Coli in profusion.

As the case progresses the temperature gradually becomes lower and the pain decreases in intensity, frequency and pain on micturition lessen, and in five to fourteen days the signs and symptoms disappear; but B. Coli may still be found in the urine, and relapse may occur just as one thinks the patient is cured. This is especially seen in pregnancy cases. On the other hand, the case may drag on with severe constitutional disturbance due to toxæmia, the patient becomes emaciated, the pulse rapid, though the

temperature may not be unduly high, and jaundice may appear.

In the mild cases there is a dull, aching pain in the loin made worse by movement. The constitutional symptoms are slight, and these cases may pass unrecognized unless a catheter specimen of urine is examined, when B. Coli, pus-cells and casts will be found. These mild cases occurring during pregnancy often give rise to an erroneous diagnosis of toxic albuminuria, owing to the presence of albumin in the urine, the lumbar pain and general malaise, but the blood-pressure is not raised and the blood urea is within normal limits.

Turning to the treatment of these conditions. In acute pyelonephritis rest in bed is essential, the patient should be kept warm and a blanket bed is preferable. Diet should be "milk" and later "light." Fluids should be given freely, barley water or lemonade. The bowels should be kept open by saline purgatives. Medicinal treatment consists in first rendering the urine alkaline by giving 30 grains each of sodium bicarbonate and potassium citrate every two hours until this is accomplished, and then every four hours for seven days. By this time the temperature is usually normal and the acute symptoms have subsided. Now is the time to turn the reaction of the urine back to acid and give a urinary antiseptic, and for this purpose acid sodium phosphate 30 grains and hexamine 10 grains t.d.s. are given. One practical point arises here: the hexamine and acid sodium phosphate, if given in a mixture, often cause sickness, due to giving off free formalin in the medicine bottle, and therefore it is better to give them separately. My usual practice is to give

the hexamine in tablet form, and at the same time give a mixture of—

Acid Sodium Phosphate	30 grains.
Tincture of Hyoscyamus	10 minims.
Infusion of Buchu	To 1 ounce.

When giving hexamine the barley water and lemonade should be stopped and plain water substituted.

As a complement to medicinal treatment local treatment is carried out, and this is especially indicated in those cases which fail to clear up under the intensive alkali treatment. The bladder is emptied by catheterisation and 2 oz. of 1 per cent. mercurochrome are instilled, and the patient instructed to hold this as long as possible. If dysuria is still present it is better to commence with ½ per cent. mercurochrome to see how this is tolerated. I believe Mr. Walters originated this form of treatment, and has found it to be nearly as efficacious as instillation of the dye into the pelvis of the kidney. I should be glad to hear his present views on the subject.

I have found it to give good results in non-pregnant cases and in the puerperal form, but not in the pregnancy pyelitis, and this is to be expected, as the pregnancy type is associated with atony and obstruction of the ureters.

Lately I have tried pyridium in these cases, and the results have been encouraging. Two tablets of pyridium are given t.d.s. at first, and later this is reduced to one t.d.s.; while giving this the fluid intake must be reduced to the minimum. I have not found any ill-results, even when given during pregnancy, except the production of nausea and vomiting in a certain number of cases. Reduction of the dosage stops this.

In treating pyelitis of pregnancy exactly the same

routine is carried out. While in bed the patient is encouraged to lie on the opposite side to the affected kidney, with the idea that it relieves pressure on the ureter.

If the aforementioned treatment fails to cure, then catheterisation of the affected ureter should be carried out. This drains the obstructed ureter and pelvis, and restores the kidney function to normal. By this means many a pregnancy has been preserved which otherwise would have had to have been terminated. If this fails to cure, then some more serious lesion of the kidney should be suspected, such as a suppurative pyelonephritis or calculus.

If all treatment fail, then evacuation of the uterus, as a preliminary to further treatment, must be carried out. If near term induction of premature labour is indicated, but if in the earlier months, then I think the best procedure is hysterotomy. Pyelitis of pregnancy rarely occurs before the fifth month, and evacuation of the uterus at this period of gestation via the vagina is a tedious process, is liable to be attended with mild infection before the fœtus is discharged, and this, as well as the time element, is important, as by the time evacuation of the uterus is decided upon the condition of the patient is usually grave. The uterus having been evacuated, then routine treatment is carried out, usually with rapid success.

Chronic Pyelonephritis.

This is more common than one would expect, and is frequently diagnosed as chronic cystitis, with which it is almost invariably accompanied, the nephritic origin of the bladder inflammation being unrecognized. The primary attack usually occurs at some previous

pregnancy, and this attack, though apparently cured as far as clinical signs and symptoms are concerned, leaves the patient with a persistent or intermittent bacilluria or some permanent damage to the pelvis or narrowing of the ureter from stenosis. Dodds, in a recent paper, gave the results of re-examination of 79 of 124 patients who had pyelitis during pregnancy on the puerperium, and of these 79, 49 had either a chronic pyelitis or bacilluria alone, that is, over 50 per cent. of the cases. All these cases cleared up under treatment, usually within six months of delivery.

The patient suffering from chronic pyelonephritis is free from symptoms for long periods, though during this time she may pass B. Coli in the urine, and then suddenly she has a subacute attack with pain in the loin, frequency of micturition and dysuria. The constitutional disturbance is slight, and one frequently sees these cases in the out-patient department. On examination there is pain and tenderness in the costo-vertebral angle of the affected side, the kidney is not palpably enlarged and there is no rigidity. There may be some tenderness over the bladder and some pouting of the urethral mucus membrane at the meatus, and sometimes excoriation of the vulva from the highly acid urine.

A catheter specimen shows high acidity, a small amount of pus, usually only on microscopic examination, which also shows the presence of the organism and some epithelial cells and perhaps casts.

On cystoscopic examination the only particular feature is the pouting of the ureteric orifice on one or both sides with a surrounding zone of inflammation.

Under treatment the symptoms subside, but the bacilluria may persist, and repeated subacute attacks are common.

Here we are faced with a much more difficult condition to cure. The usual routine treatment carried out in acute cases will relieve the subacute exacerbations, but a permanent cure by these means is unusual, hence the multiplicity of advertisements for urinary antiseptics which litter our breakfast tables.

In some cases urinary antiseptics, such as hexamine, pyridium, caprikol and hexyl-resorcinol, to mention a few, may affect a cure, but in the chronic cases local treatment of the pelvis of the kidney or kidneys is indicated. The pelvis of the kidney is drained by ureteric catheterisation and the antiseptic instilled into the pelvis; for this purpose mercurochrome or some silver preparation may be used.

As an aid to treatment vaccine therapy may be tried. An autogenous vaccine is the best, commencing with half a million organisms and working up to 250 million, given at intervals of four to seven days, depending upon the reaction obtained.

The latest addition to our armamentarium is the ketogenic diet, which was elaborated by Clark at the Mayo Clinic. The growth of the B. Coli has been shown to be inhibited by raising the acidity of the urine to a high degree, and this is accomplished by giving a diet in which fat forms the major portion, with a very small amount of carbohydrates and protein. The actual amounts are: fat 250 grammes, protein 78 grammes, and carbohydrate 25 grammes.

Ammonium nitrate 80 grains daily is given orally to increase the acidity. The result of this is to produce a high acidity and ketonuria, which, according to the writer, clears up the condition in about twenty-one days after the production of the ketosis. During treatment the patient should carry on a moderate

amount of work or a prescribed amount of exercise, in order to oxidize the fat.

It is obvious from the nature of the treatment that the person must be physically fit to stand this diet, and be able to metabolize this amount of fat; moreover, it is obviously contra-indicated in pregnancy and the puerperium, and it seems to me that it is more suitable for males than females. Personally, however, I have had no experience of this form of treatment, and I should be grateful for more information from others who may have employed it.

I am afraid that I have added nothing new to this subject, but have tried to put before you the present state of our knowledge of this type of infection in the female, more especially that occurring during pregnancy.

THE USE OF THE VENTRAL POSITION IN THE TREATMENT OF TUBERCULOUS DISEASE OF THE SPINE IN CHILDREN.*

BY

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IT is very difficult to discuss the treatment of tuberculous disease of the spine, as the treatment is so lengthy and the results so distant and so easily modified by the future home and social conditions of the patient.

It is easy to produce destructive criticism of the accepted methods of treatment, but very hard to suggest any treatment which is an improvement on the standard methods.

The disadvantages of the treatment of cases by some modification of the double abduction spinal frame can be considered under the following headings :—

1. General condition and comfort of the child.
2. The muscular system.
3. The skeletal changes.

* Reprinted by permission from the Annual Report for 1932 of the Medical Officer of Health for Bristol.

1. The child treated on a double abduction frame can do very little for itself, its education is very limited, the direct line of vision and, consequently, its outlook on life is limited to a white ceiling or a blue sky. Its external surroundings have to be viewed through a mirror or after contortions of the neck. In the supine position mental concentration is difficult and reading becomes very tiresome, writing for any length of time an impossibility.

2. One or two years' treatment on a spinal frame causes a marked generalized wasting of the muscles of the body, especially those of the erector spinæ group. The skin becomes slightly œdematous over the outer and posterior parts of the thigh and trunk. During the cold weather the efforts of the child to draw the legs together to keep warm tends to produce knock-knee. In spite of the constant efforts of the masseuse the leg muscles waste. Great care has to be taken in the nursing of these cases to prevent hyper-extension of the knees, foot-drop, stiff knees and hips.

In many cases the disuse atrophy is so extreme that the convalescent period has to be prolonged, the time being spent in muscular development and re-education, and finally some form of posterior spinal brace has to be worn to take the place of the atrophied posterior spinal muscles.

3. Prolonged treatment with absolute immobilization causes marked decalcification of all the bones of the body; added to this there is the local decalcification due to the tuberculous lesion.

PLATE IX

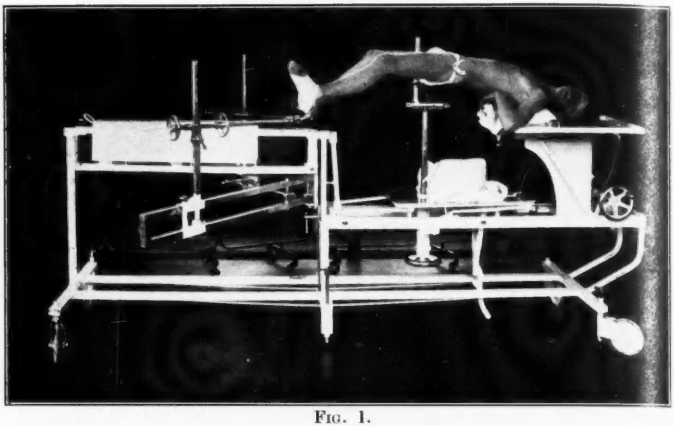


FIG. 1.

FIG. 2.

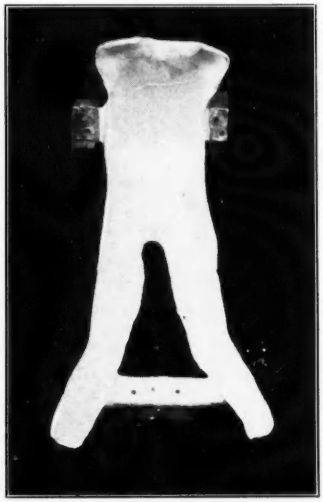


FIG. 3.

This marked decalcification, attended by an increased excretion of calcium from the body, seems to predispose to renal calculi.

There is often a marked flattening of the chest from before backwards in those children that have been treated in spinal frames for several years. This is accompanied by a lateral spreading of the ribs, which gives the patient a very peculiar appearance. This must be due to the weight of the body on the very decalcified ribs.

In order to overcome these defects of the frame treatment I have been treating cases of tuberculous disease of the spine in children where the disease has been situated in spinal segments between the mid-dorsal and lower lumbar regions in the prone position in plaster hyper-extension beds.

The method of construction of the plaster beds.

The child is placed on an orthopædic table as shown in Fig. 1. The front of the abdomen and legs are coated with ung. zinci et ol. ricini. One layer of plaster bandages is applied to the front of the child, the rest of the case is made from pressed slabs of plaster, which are applied till the whole case is about $\frac{3}{8}$ in. thick. This is removed and cut to the correct shape. The feet are then fixed on the cast. The inside is polished till it is smooth. The case is then dried and afterwards varnished with cellulose varnish.

If the case is carefully made no padding is needed, in fact the children are more comfortable without it. The plaster beds are screwed to the galvanized iron top of the ordinary beds.

Important points in the construction of the plaster beds.

The legs are abducted, the knees slightly bent to prevent the knee ever becoming fully extended. The child is secured to the bed by a bandage round each thigh and round the lumbar region. From the knee downwards the child can move the legs as much as he pleases. There can be no tendency to develop drop-foot, knock-knee or hyper-extension of the knee.

A certain movement of the spine is possible in the direction of increased hyper-extension, the plaster prevents flexion and lateral movement. The constant muscular effort of lifting the head and shoulders develops the posterior spinal muscles to an extraordinary degree, and these muscles are more efficient than any spinal brace during the convalescent stage.

Figs. 2 and 3 show a plaster bed as it is when finished. Slight modifications are made when the lesion is in the mid-dorsal region; in these cases a head rest is made, as shown in Fig. 4. When the lesion is situated in the lumbar region no head-rest is fitted.

Figs. 5 and 6 show the patients in the plaster beds; a small bed table is provided in front of the child, on which the patient can rest his arms, and on which two pillows are put for the head to rest at night.

Duration of treatment in plaster beds.

When the disease appears to be quiescent, as shown by temperature chart, radiological examination,

PLATE X

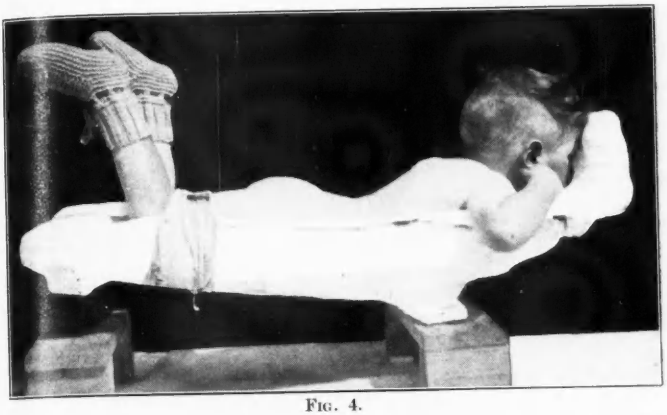


FIG. 4.

FIG. 5.

FIG. 6.

and good compensating curves have developed, the child is taken out of the plaster bed and treated in the prone position during the day, with a triangular pillow under the upper part of the trunk, to maintain the hyper-extension of the spine. During the night they are allowed to sleep on their backs. During the periods when children are free in bed exercises are performed every day in the form of leg movements.

This trial period lasts at least three months, and should the child progress satisfactorily, it is then allowed crawling exercises, and finally to walk.

During the convalescent period the child is either in the prone position or walking. Great care is taken to prevent the child sitting or standing about. They attend school, and are taught in the prone position on canvas stretchers.

CONCLUSION.

Comparing my series of cases, about half of which have been treated in the prone position as outlined above, and the other half in the dorsal position in double abduction frames, I find:

1. The children are happier in the prone position, they eat better, do the school work better, and need less attention.

2. Their general muscular tone is splendid. Their compensating curves develop much more quickly, there is no stiffness of the knees, limited movement, or weak ligaments, even after two years of treatment.

There is not such marked generalized decalcification as one finds after even short periods of frame treatment.

3. The average duration of treatment in uncomplicated cases is reduced by one-third.

4. No spinal brace has to be worn.

BRISTOL UNIVERSITY: DEPARTMENT OF PREVENTIVE MEDICINE.*

OPENING BY THE MINISTER OF HEALTH.

On Friday, 29th September, the Minister of Health, Sir Hilton Young, formally opened a new Department of Preventive Medicine at the University of Bristol. The Department is housed in Canynge Hall, which has been adapted and equipped for the purpose. Under an agreement between the University and the city the bacteriology, pathology, and preventive medicine work of Bristol and its municipal hospitals will be carried out by this Department, which will receive a grant from the city for its maintenance. In order to facilitate arrangements Professor Walker Hall resigned his Professorship of Pathology and was appointed Director of the new laboratories, and Dr. R. H. Parry was appointed Honorary Professor of Preventive Medicine in the University. The vacant Chair of Pathology has been filled by the appointment of Professor G. Hadfield of the Royal Free Hospital (formerly Pathologist to the Bristol General Hospital), who will devote himself to research and teaching. The promised co-operation of the pathologists at the Royal Infirmary and the General Hospital will enable Professor Hadfield to draw his material and give instruction to his classes in those two institutions.

* Reprinted by kind permission of the Editor from the *British Medical Journal*, 7th October, 1933.

The association of the Preventive Medicine Department with the municipal hospitals at Southmead, Ham Green, Frenchay and elsewhere will likewise serve to increase the material to which medical students and research workers in Bristol will have access. The Professors of Medicine, Surgery and Obstetrics are also accommodated in Canynge Hall, so that for the present all academic lectures in the clinical subjects will be given there.

At the inauguration ceremony the Vice-Chancellor, Dr. Thomas Loveday, welcomed the Minister of Health in the large Lecture Theatre before a considerable assembly of guests, including the Lord Mayor of Bristol, the Sheriff (Dr. Kenneth Wills), Alderman Maggs (Chairman of the Health Committee), Dr. Stanley Badock (Chairman of the University Council), and Mr. Hiatt Baker (Pro-Chancellor).

Dr. Loveday described the steps by which the connection between the City Health Services and the University Pathological Department had grown up during more than thirty years, until it had culminated in this complete union in the Department of Preventive Medicine. It was, he said, a difficult experiment to start, but it would be easy to carry on when well started. Both parties to the agreement expected that it would work happily under the direction of Dr. Walker Hall, with the Medical Officer of Health, Dr. Parry, in the Chair of Preventive Medicine.

Alderman Maggs, as Chairman of the Health Committee, said he looked upon this development as a great step forward in the interests of the public health for the protection of food supplies, for the earlier recognition of disease and for its control and treatment.

Sir Hilton Young, declaring the new Department open, referred to the tour of Bristol he had just

made—viewing the new housing estates, the city's efforts at slum clearance, the homes for children, the nursery school, the municipal hospitals, particularly the Orthopædic Hospital at Frenchay and Hortham Colony for Mental Defectives. He congratulated the city on feeling forward along the lines of development of the public health services and grasping at new opportunities. Bristol had its slum problem, a legacy of old days with lower standards, but it had also its legacy of traditional progress. "This Department of Preventive Medicine will stand as an example of vigour and foresight adequate to your needs. It should give to everyone encouragement and high hope to continue the efforts of a great and honourable past."

Dr. Walker Hall and Dr. Parry also spoke, each paying tribute to the great preventive work carried out by the late Dr. D. S. Davies, who for many years was Medical Officer of Health for Bristol.

Dr. S. Badock proposed a vote of thanks to Sir Hilton and Lady Young, and referring to Sir Hilton Young's remark that the present celebration was a marriage of the City of Bristol with the fair nymph of knowledge, said that it was a most modern type of marriage, in that it was subject to revision from time to time, but this provision would probably achieve a lasting and happy union.

After the opening ceremony the Minister of Health was the guest of the University at lunch in the University Union. The Lord Mayor (Councillor Wise), in the course of his speech proposing the health of Sir Hilton and Lady Young, mentioned with pride that Bristol possessed an example of Lady Young's artistic handiwork in the Cathedral.

Sir Hilton Young, replying, said that he would not

have asked for this opportunity of paying Bristol a visit if he had not been confident that he would find there a discharge of the services for which he was responsible that was in the best standard of national achievement. "I can confirm from my personal impressions and knowledge," he said, "that you need not fear comparison with other great cities of the country."

Dr. Middleton Martin, Medical Officer of Health for Gloucestershire, spoke of the value to the county in the past of the University's Pathological Department, and welcomed this extension as promising to be of even greater service in the future. He, like other speakers, referred to the splendid work of the late Dr. D. S. Davies.

Undoubtedly the occasion marks a further stage in the closer co-operation between the State and voluntary organizations which is all to the good. It is perhaps singular that throughout the proceedings no speaker mentioned Bristol's greatest contribution to preventive medicine in the discovery by Dr. William Budd of the mode of transmission of typhoid fever. Dr. Budd's rules for nursing typhoid cases are to this day employed by the whole civilized world.

Reviews of Books

The Medical Annual for 1933. Edited by the late CAREY F. COOMBS, M.D., and A. RENDLE SHORT, M.D., B.S., B.Sc. Pp. civ., 628. Illustrated. Bristol: John Wright & Sons, Ltd. 1933. Price 20s.—The interest of the present volume is indeed well maintained, for there is hardly a page which does not give a new suggestion as to treatment or describe some new form of disease. We entirely agree with the opinion quoted that "probably every doctor in active practice sees each year at least one case that can be better diagnosed or treated if he is aware of the advances on the subject recorded in recent numbers of the *Annual*." Among the surgical novelties noticed are the removal of parathyroid tumours for osteitis fibrosa, the surgical treatment of detached retina and of pulmonary diseases by phrenicotomy. Many readers will be thankful for the complete table of doses for the New Pharmacopeia as given here, and for the summaries of recent work on the vitamins and on rheumatism. Moynihan's instructions to patients after gastric operations is another thing which we should like to keep by us always, especially with the amusing misprint which forbids patients to indulge in "high games" instead of high game as food. Attention is drawn to the startling results of the treatment of malaria by atebrin, and to the danger of aperients and even of enemata in pneumonia. The *Annual* has suffered a great loss by the untimely death of Dr. Carey Coombs, and we are sure that all readers will sympathize with the brief but affectionate tribute to his memory on page 8.

Royal Berkshire Hospital Reports, 1932 and 1933. Edited by H. S. LE MARQUAND, M.D. Illustrated. Reading. 1932 and 1933. Price 10s. 6d. each.—It is a new departure for a provincial hospital to publish annually a volume of collected papers, and the medical staff of the Royal Berkshire are to be congratulated, both on the form of these volumes and on the high standard of the contributions. The object of the *Reports* is to preserve permanent records of much useful information at present buried in the hospital notes, and

secondly to supply the neighbouring practitioners with information relating to new methods of diagnosis and treatment. Many of the contributions will be of special interest to pathologists, whilst to the general practitioner we would especially commend Dr. John Mills' article on Glandular Fever (1932) and the very clear, simple and informative description of electrocardiograms and their interpretation by Dr. G. Lambert (1933). The next two volumes will be published together in 1935.

The Thyroid Gland. By C. R. HARINGTON, Ph.D., F.R.S. Pp. xiii., 222. Illustrated. London: Oxford University Press. 1933. Price 15s.—The avowed intention of the author of this volume is to give an account of the thyroid gland as it appears to the chemist: to do this it has been necessary to make incursions into the fields of physiology and pathology. Dr. Harington has given much time to researches on the thyroid gland, especially with regard to more satisfactory methods for the isolation of thyroxine, and, like all research workers, he has become thoroughly acquainted with the literature of his subject, and this acquaintance renders his monograph extremely valuable to all interested in the thyroid gland from various points of view. Although it is not written especially for clinicians, it should be of considerable use to physicians, since it contains an account of investigations on the thyroid gland from early times to the present day, and also an alphabetical list of authors who have dealt with this subject. It is interesting to observe that as far back as the thirteenth century goitre was treated by the administration of burnt sea sponge—some five or six hundred years before the isolation of the element iodine. The chapter on the chemistry of thyroxine is up to date, and should interest students of biochemistry, and the concluding chapter on the biological aspects of Graves's Disease should appeal to physiologists and practising physicians, and stimulate the latter to develop some satisfactory medical means of treating this condition. A number of interesting photographs are included to illustrate the effects of deficient thyroid secretion in human beings and in the lower animals. We congratulate both author and publisher on a treatise which should be of great value.

Nervous Disorders in Infancy and Childhood. By NEILL HOBHOUSE, M.D. Pp. viii., 212. London: H. K. Lewis & Co. Ltd. 1932. Price 8s. 6d.—The nervous complaints of children have not received as much attention in the medical literature

of this country as has been afforded to them elsewhere, and Dr. Hobhouse has done a service to the practitioner in preparing this concise, lucid and readable volume. He describes most of the nervous syndromes which are met with in childhood in non-technical terms, so that even the practitioners who do not profess neurology may approach the book with confidence that they will not lose themselves in a sea of jargon. Naturally there are some points which will not meet with universal acceptance, such as his adherence to Stoeffel's operation for spastic paralysis (which produces such dramatic immediate improvement, but which is often attended by dire results in the form of obstinate contractures later on), but this is inevitable in any up-to-date medical work. The chapter on hyperkinesis is valuable inasmuch as he lays stress on the differentiation between tricks and tics and chorea proper, and makes it clear to the practitioner that while rest is essential for the latter it is the worst possible treatment for the former. There are two final chapters on psychoneuroses and mental defect which do not pretend to be adequate to their subject, but they are sufficient to indicate to the practitioner what he may be up against and may encourage him to seek further information elsewhere. Altogether a book to be commended.

Paralysis in Children. By R. G. GORDON, M.D., D.Sc., and M. FORRESTER BROWN, M.D., M.S. Pp. viii., 328. Illustrated. London: Oxford University Press. 1933. Price 15s.—This book has been written from the combined aspects of the neurologist and the orthopædic surgeon. This is a very sound idea, as each has so much to contribute towards the treatment of most cases of paralysis. It has been divided into three sections. The first outlines those general anatomical and physiological considerations without a due appreciation of which rational diagnosis and treatment are impossible. It contains many useful diagrams designed to refresh the memories of those of us whose recollections of the anatomy of the central nervous system have become a trifle hazy. The second section is considerably the longest. An account is given of each type of paralysis, which is then further illustrated by clinical records of cases. This section forms a most useful work of reference, and by itself fully justifies the publication of the whole book. The third part concerns treatment, and here the authors must have had a hard task to decide what to include and what to omit. On the whole they have exercised excellent discrimination by insisting upon principle rather than upon

detail. For the latter some larger tome of orthopædic surgery must be consulted when necessary. The authors have deliberately repeated themselves in certain parts of the text, as is almost unavoidable in a work of this sort. A considerable number of the illustrations have also been duplicated, and this seems to the reviewer to be a mistake. If every illustration were exactly opposite the text it might be worth while, but this is not so. If one has to turn any pages the exact number makes little difference. As with all the Oxford Medical Publications this is a well-printed volume of handy size. It is well indexed.

The Adjustment of Muscular Habits. By JAMES K. MCCONNEL, M.C. Pp. xi., 129. London: H. K. Lewis & Co. Ltd. 1933. Price 4s. 6d.—This little book is an extremely interesting one, and deals with a subject of great importance to all branches of the medical profession. During the last few years the attention of the profession, as well as of the public through the lay Press, has been drawn increasingly to the significance of postural defects—poor body mechanics, as our colleagues in the United States of America call them, but the chief stress has hitherto been laid on their mechanical aspects, somewhat to the neglect of the human or psychological side. It is evident that since the publication of his earlier book on *Shorter Convalescence* Colonel McConnel has been struggling with the problem, which confronts all workers in physical training, *i.e.* how to make the patient who feels comfortable in a poor attitude wish to replace it by a correct one, and how to convert a voluntary and temporary correction into a permanent, automatic balance. The author is obviously a successful practitioner in this art, and he endeavours in this book to impart the principles which he has found valuable in overcoming what is no easy problem. As a simple illustration of the psychological requirements, he points out that "one bite on an exposed dental nerve, or a cut in the pad of a finger may change abruptly the habits of a life-time," and also "our muscular behaviour varies with conditions, such as the stimuli, the environmental and internal circumstances." Accordingly "we must not confine ourselves to the motor aspect of habits, when we desire to substitute good muscular habits for bad ones." He further points out that many primary bad habits exist without giving rise to symptoms, due to the remarkable resistance of our bodily tissues, and only when resistance is reduced does disability occur, which causes most treatment to be directed to raising the resistance without correcting

the faulty habit; whereas efficient treatment demands the elimination of both factors. A common example of this is the faulty postural and respiratory habit that follows recumbency after an abdominal operation, and which so seldom receives attention by either surgeon or family doctor. The author stresses the importance of enabling the patient to guide his own efforts by teaching him the mechanism of good and bad muscle actions and their effect on other systems of the body, and by assisting him to alter environmental conditions as far as possible, so that the initial achievement and its repetition may take place under conditions peculiarly favourable to it. Amongst external conditions *incentive* is one of the most important, and, of course, varies with different individuals. Another point often overlooked by gymnasts is that "the criterion of efficiency is *balanced action* of the numerous muscles, each in its allotted task." Another important consideration is that "rapidity in habit formation is found to depend on *avoiding direct* voluntary control and on inducing the required muscular responses in an indirect manner." The author draws attention to another aspect of the problem, frequently neglected, *i.e.* the interaction of various postural defects, so that it is rare for one to exist alone, and further that it is only by laying the responsibility for progress on the patient, instead of allowing him to rely on outside help, that we can avoid relapse, which is so common in these defects. Such are the main outlines of the author's thesis, and his book is well worth thoughtful perusal by members of every branch of the profession.

Treatment of Rheumatoid Arthritis and Sciatica. Second edition. By A H DOUTHWAITE, M.D. Pp. xii., 131. Illustrated. London: H. K. Lewis & Co. Ltd. 1933. Price 6s.—This book deals with the treatment of rheumatoid arthritis as distinct from septic arthritis and osteoarthritis. So much emphasis has been laid on the part played in the causation of the disease by septic foci that it is interesting to note that the author does not regard sepsis as the most important ætiological factor, and lays emphasis on the fact that at least equal attention must be paid to endocrine disturbances, vitamin deficiencies and metabolic changes. Amongst newer methods of treatment which are described attention should be paid to the use of arthrytin and allochrysine during the first stage, to the use of splints and of wax during the second stage, and the necessity for manipulative treatment

during the third or non-progressive stage. In the portion of the book devoted to sciatica Dr. Douthwaite makes it evident that successful treatment must depend on correct diagnosis of the nature and site of the sciatic lesion, whether it be primary or secondary, peripheral or central. Most encouraging results are reported from epidural spinal injections and from spinal manipulation, and the author concludes that we should be able to look forward with confidence to a steady diminution of sufferers from chronic sciatica, which can now but rarely be described as intractable.

Chronic Rheumatism and the Pre-rheumatic State. By J. H. HINDLEY-SMITH, M.R.C.S. Pp. 154. London: H. K. Lewis & Co. Ltd. 1932. Price 5s. 6d.—This is a misleading and from its very simplicity a dangerous book. The author groups all chronic rheumatism together without any sort of clinical distinction. He states that the chronic rheumatic infection of childhood leads to an instable delicate condition in adolescence, and a state most closely resembling secondary rheumatoid arthritis in middle life, that these are all due to pharyngeal infection with a streptococcus, and that chronic rheumatism can be prevented and cured by a special regime, the chief features of which are vaccines and ultra-violet rays. The doses of vaccine suggested are considerably in excess of those recommended by recognized authorities at the present day. It is to be hoped that practitioners will not be misled by the convenient and simple panacea here presented, for chronic rheumatism is a complex and difficult subject, and the various clinical conditions included under this term are due to a variety of etiological factors, and consequently require a variety of therapeutic measures. There are no short cuts in medicine, and though the wish is often father to the thought, such wishes are not to be trusted.

Diseases and Disorders of the Digestive Organs. By ADOLPHE ABRAHAMS, O.B.E., M.D., F.R.C.P. Pp. vi., 110. London: John Bale, Sons and Danielsson Ltd. 1932. Price 2s. 6d.—This is a most excellent pocket monograph, illuminated with an occasional touch of humour, a welcome ray too infrequently shed on medical writings. Not that the subject is treated lightly; on the contrary, for its size the little book is very comprehensive. The diagnosis of gastric ulcer is rather weak: the merits of medical and surgical treatment are helpfully compared, and the all too frequent

inadequacy of the former is very pointedly emphasized. The standard of time generally accepted as required for such should be readjusted; the public and the profession as a whole are not alive to this as they are in respect of tuberculosis. Moreover, the farcical futility of attempting any ambulatory treatment for gastric ulcer is expressed, and with reason; "rather a patient on a comparatively generous diet but strictly confined to bed than prosecute the most elaborate procedures with diet and drugs whilst allowing physical activity." The probability of an ulcer diathesis, once an ulcer has been established, though healed, is very properly urged. The views expressed are wrapped in common sense: this is generally obvious and welcome in a well-balanced preamble to a discussion of the diagnosis of cancer of the stomach, and in a section devoted to nervous indigestion.

Some Thoughts on Asthma. By A. J. D. CAMERON, M.B., Ch.B. Pp. viii., 178. Illustrated. Bristol: John Wright & Sons Ltd. 1933. Price 7s. 6d.—Dr. Cameron's monograph on asthma gives his views on the production of the disease, and demonstrates the method of treatment carried out at the Sherwood Park Clinic at Tunbridge Wells. He describes it as the Haseltine treatment, and the book is full of his own experiences relating to the causation and treatment of the disease. The etiology of asthma is traced through its stages up to the final stage of bronchospasm. The fundamental origin is a basic toxicosis arising from the liver and intestines, these produce or are linked up with septic foci in the ethmoid region, or may be from teeth, gall-bladder, appendix, etc., which produce a state of irritability of the nervous system, a vagotonia which results in the attack of bronchospasm. Dr. Cameron describes the treatment of each stage. This is a monograph which will interest the medical practitioner. Though some of the treatment is best carried out at a recognized spa institution, in certain cases Dr. Cameron thinks it should be possible adequately to deal with it at home, provided the patient could be sent to a treatment centre daily.

The Injured Workman. By G. F. WALKER, M.D., M.R.C.P. Pp. xix., 190. Bristol: John Wright & Sons Ltd. 1933. Price 6s.—Most qualified men and women, whether in general or consultant practice, are called upon at one time or another to attend a court of law for the purpose of giving evidence in compensation cases. This may prove to be a difficult task for those who are not constantly doing this type of work, and

may be a source of some anxiety. The book under review should be of the greatest value to the occasional medical witness, and solves many of his difficulties. There is a Foreword by Professor Maxwell Telling, which alone is most illuminating, the book itself being written in collaboration with four consultants, including a barrister-at-law. The opening chapter deals briefly with the law relating to the Workmen's Compensation Act, and advises the medical witness as to his conduct in court. This is followed by chapters on the more common accidents to workmen, their results and complications and warnings of the mistakes into which the unwary may be trapped. The subjects are dealt with systematically, injuries to the ear, nose, throat and eye are included. There are also a few words of advice on the all-important subject of malingering. The book is recommended with the utmost confidence.

Practical Food Inspection. Volume 2. By CHARLES R. A. MARTIN, M.R.S.I. Pp. vii., 249. London: H. K. Lewis & Co. Ltd. 1933. Price 10s. 6d.—This volume deals entirely with foods other than the meat of animals killed in slaughter houses, and with the first volume makes the work complete. It is intended not only for students qualifying to undertake the duties of meat and food inspectors, but also for meat and food inspectors generally, and will be found useful to executive officers whose duties comprise the supervision of our food supply. The author has dealt with the subject lucidly and is up to date with our present knowledge of the various diseases affecting fish, poultry, and also vegetables and fruit. The principles governing expert examination, and the methods of detection of unsoundness are enunciated. The reasons for the deterioration of food and the manner in which any departure from the normal may be expected to take place are also indicated. The book is capably illustrated from drawings made by the author himself, and concludes with a glossary of terms and a very clear index.

The Sanitary Inspector's Handbook. By HENRY H. CLAY. Pp. xx., 386. Illustrated. London: H. K. Lewis & Co. Ltd. 1933. Price 15s.—Practical handbooks by sanitary inspectors for sanitary inspectors are few, and when it was known that Mr. Clay had undertaken to replace Clarke's handbook with an up-to-date edition the publication was eagerly anticipated and the work eminently fulfils all expectation. The author

was an expert sanitary inspector before he graduated to his present position on the staff of the London School of Hygiene and Tropical Medicine, and thus writes on a subject of which he has a masterly knowledge. The arrangement of the book is very good, commencing with an epitome of the evolution of the sanitary inspector's calling. The different phases of the inspector's duties are sub-divided, each chapter completing a particular subject. An important feature is that where the appropriate legal enactments have to be given they are interspersed with lucid explanatory notes, thus rendering the study of statutory powers not only easily readable but interesting. The illustrations, of which there are a large number, are clear and concise, showing the various methods of construction and the latest type of sanitary fittings. It has a very complete index. The work will rank as the standard text-book on the subject for the practising inspector as well as the student sanitary inspector.

Stoke Park Monographs on Mental Deficiency. No. 1. By RICHARD J. A. BERRY, M.D. Pp. xix., 249. Illustrated. London: Macmillan & Co. 1933. Price 10s. 6d.—The book is issued as a memorial to the late Rev. H. N. Burden, who founded and equipped at his own expense the National Institutions for Persons Requiring Care and Control, now housing nearly 2,000 patients. The full scope of the volume is not indicated by the title, as work is described carried out elsewhere than at Stoke Park. Some articles are for the student and others for the specialist. Of the articles published for the first time Berry and Norman describe the brain changes of three defectives. Norman contributes an interesting paper upon neurological findings. Cerebellar ataxia is described elaborately by Bates and Berry, but the excellent results of treatment are discussed too briefly. The observations recorded in the volume should prove of value to those with little knowledge of mental deficiency, but too much reliance must not yet be placed upon all the conclusions drawn from the observed facts. The volume is up to date and attractively produced, the illustrations are good, the references full and the index detailed.

Psychology of Sex. By HAVELOCK ELLIS. Pp. xii., 322. Illustrated. London: William Heinemann, Ltd. 1933. Price 12s. 6d.—The aim of this book is to present in concise form the essentials of a subject which enters into everyday practice and is receiving wider and wider attention. Routine

medical teaching leaves the student almost entirely uninstructed in the bare elements of sex psychology. When he goes into practice he is at a loss when trying to deal with obvious problems in this field. The reason for this hiatus in medical education is clear, the subject-matter is unsuitable for ordinary bedside teaching. The book sets out in simple language the biological and social aspects of sex life from the psychological standpoint. The writer confines himself to facts disentangled from psychoanalytic theories. Particularly helpful is the chapter on marriage, which affords a basis for helpful advice and instruction to patients. Every practitioner will find in the book a great deal of information that he ought to know and a great deal that he can hand on to patients, when properly called upon to do so. Sympathy and common sense is wanted in a high degree in dealing with sex problems: there is little hope of achieving either in the absence of accurate knowledge of the subject. The book can be strongly recommended to both practitioner and student.

Human Values in Psychological Medicine. By C. P. BLACKER, M.C., M.D., M.R.C.P. Pp. ix., 179. London: Oxford University Press. 1933. Price 8s. 6d.—Nowadays philosophy is concerning itself to an increasing extent with the subject of values. Heretofore medicine—even psychological medicine—has not concerned itself with this field of thought. A short review of the older philosophic conceptions of values is given, and Dr. Blacker then seeks to define his own conception of value. He thinks that it is to be derived from Macdougall's "essential and permanent nucleus of the instinct," and that the true basis of human valuation is to be found at the instinctive level and not in derived experience, though it may of course be modified by this. The significance of the individual is to be found in his idiosyncrasy, *i.e.* the particular "private mixture" of characteristics, especially mental, which differentiates him from his fellows. It must be remembered, however, that it is extremely difficult to describe such idiosyncrasies verbally, and the meanings used by psychologists are as a whole very difficult to convey in words at all.

In mankind values have been largely modified by socialization, but it might be expected that individuals will have individual "pivotal" values, *i.e.* that there will be something which is of major importance in their lives. The author has investigated this subject, and has found that his patients divide themselves into four groups: (1) Those who

have no pivotal values, and are unconscious of ever having needed them; (2) those who have in fact pivotal values, but have never consciously needed them; (3) those who have needed such values, and have found them without much difficulty; (4) those who have consciously needed such values, and have had difficulty in finding them. The latter group tend to be neurotic. The author discusses various religious and philosophic valuations, and compares them to neurotic and psychotic reactions, and then goes on to discuss the difficult problem of reality at some length. This book undoubtedly contains much of interest, and the philosophical approach to psychiatric problems is unquestionably a valuable one. It is probable that many medical men, who are neither trained nor interested in philosophy, will be repelled by this very approach, but that is their misfortune and not the author's fault. None the less, there is a tendency to diffusion and following up of side-lines, no doubt interesting in themselves, but not strictly germane to the argument, which detracts from the value of the book as a serious contribution to psychopathological literature.

Neurology—Psychiatry. Practical Medicine Series. Edited by P. BASSOE, M.D., and F. G. EBAUGH, M.D. Pp. 471. Chicago: Year Book Publishers Inc. 1931.—This annual production is always to be welcomed. It consists of a series of articles from the medical literature of the world on Neurology and Psychiatry. Being an American publication, it is to be expected that American work looms most largely in the selection, but that is of advantage rather than of disadvantage to Neurologists and Psychiatrists working "on this side." The selection is comprehensive, but as inevitably happens, it is the frequent experience of the seeker for information that what he particularly wants is not there. However, if such subject-matter is not dealt with one year it almost certainly will appear another. The editorial comments introduced by Dr. Ebaugh in the psychiatric section are of definite interest and value. There can be no question that this and its companion volumes should be at the command of all serious students of the subject.

Diseases of the Nervous System. By W. RUSSELL BRAIN, D.M. Pp. xvi., 899. Illustrated. London: Oxford University Press. 1933. Price 27s. 6d.—The appearance of a new text-book of nervous diseases was needed at the present time. There have been a large number of important advances in neurology in

the last ten years which had yet to be incorporated in current text-books. The book is fully up to date, and the author seems to have left out nothing of importance. The classification of nervous disorders is always a matter of considerable difficulty. This is largely overcome by the preliminary survey of disorders of function in the light of anatomy and physiology, while in chapter vii there is an excellent review of a number of diseases from the ætiological standpoint. The reader will find that there is hardly any clinical problem which has escaped the attention of the author. Notably the book includes a useful chapter on diseases of the nervous system in relation to life insurance. An extension of this to a consideration of compensation cases would have been very helpful. The book can be strongly recommended for the use of the general practitioner and neurologist alike. The table of contents, index and bibliography are very complete and well arranged.

A Synopsis of Surgery. Tenth Edition. By ERNEST W. HEY GROVES, M.S., M.D., B.Sc. Pp. viii., 693. Illustrated. Bristol: John Wright & Sons, Ltd. 1933. Price 17s. 6d.—For twenty-five years this has been one of the outstanding successes amongst text-books for students, and it is not necessary to say much here to commend a book that has so thoroughly and deservedly established itself. The principal changes relate to the radium treatment of cancer, the Winnett Orr method of treating osteomyelitis, the surgery of the sympathetic nervous system, and amputations, all of which are excellent. Amid such a vast number of statements of fact and opinion there are, of course, some which would not command universal assent. A physician who chanced to read the section on Gastric Ulcer would be moved to indignation, and we must confess that we think the assertions made are too sweeping. The injection of A.B.A. might well be mentioned in the treatment of pruritus ani and fissure-in-ano, and radium for cancer of the thyroid. Is it not time that sarcoma disappeared from text-books amongst the alleged tumours of the breast? We are glad to see that Dr. Todd's lead selenide method of treating cancer is recognized.

A Surgeon's Pocket Book. By H. S. SOUTTAR, D.M., M.Ch. Pp. viii., 285. London: William Heinemann Ltd. 1933. Price 7s. 6d.—This work is actually a précis of Mr. Souttar's larger book on the subject of surgery, and a précis in its briefest possible form. It contains little more than headings and lists, brief notes, in fact, which the student should make for

himself. While admitting the undoubted value of such a book, which is accurate to the last word, there must be the risk that it would, and could, replace that extraction and cutting down from a complete work on surgery and from lectures which is so valuable in impressing facts on the mind of the learner. The book can easily be carried in the pocket, and might well be of service during that last and terrible fortnight preceding an examination when we are in a perpetual state of suddenly remembering something we have forgotten to look up. If the book is to be used at all in the systematic study of surgery, it must be read in conjunction with a larger work on the subject and compared with the notes which the student makes for himself, for the purpose of correction and for the estimation of the comparative values of different methods of classification. Apart from its use for examination purposes, *A Surgeon's Pocket Book* might find favour in the eyes of the qualified man, whose memory is not all that he could wish.

The Cure of Hæmorrhoids, Varicose Veins and Ulceration by Modern Methods of Injection and Bandaging. By STUART MCAUSLAND, M.D. Pp. vii., 63. Illustrated. London: John Bale, Sons and Danielsson Ltd. 1933. Price 3s. 6d.—This little volume comprises a description of all the modern treatments by sclerosing injections in a most lucid and succinct manner. The style makes easy reading, and yet there are many classifications which help the memory. In addition to discussing the pros and cons of the modern versus the old-established operative procedures, the author takes pains to define the nature of the minor maladies which the methods are intended to alleviate. In this way he protects both the doctor and patient from the pitfall of treating for piles when this condition is perhaps only a secondary subsidiary manifestation of cancerous or other serious trouble in the recto-colon. It is pre-eminently a practical guide. The procedure and diagnosis of each step in the treatment is described in every detail, so that the amateur may quickly attain the skill of the expert. The illustrations are numerous and clear.

Practical Points in Eye Surgery and Dressing. By HUGH E. JONES, M.R.C.S. Pp. 27. London: John Bale, Sons & Danielsson Ltd. 1933. Price 2s. 6d. This small volume is addressed to nurses, house surgeons and general practitioners,

the author's main objects being to assist them in the management of eye cases until expert advice can be obtained, and in the preparation, after-treatment, etc., of patients requiring operation. He provides a great deal of sound practical information in a handy form for ready reference. Three tables, contained in an envelope in the cover, are especially useful. They deal with the differential diagnosis and immediate treatment of urgent non-traumatic cases and of injuries, instruments used and drops required before and after operation, patients' diet and duration in bed, the admission of visitors, etc. The instructions are concise and necessarily rather dogmatic, but realizing that other surgeons may favour variations in some of the details, the author has provided space for additional notes. To those without special experience in the subject the book can be recommended as a most useful guide when ophthalmic problems have to be solved.

Natural Childbirth. By G. D. READ, M.D. Pp. ix., 127. Illustrated. London: William Heinemann Ltd. 1933. Price 7s. 6d.—This interesting little book discusses the problems of childbirth from a novel angle. The psychological and emotional aspects of labour are presented in a most helpful manner. The author has performed a most useful service in stressing the importance of fear as a very real factor in the causation of difficulty in childbirth. All who have to do with obstetric practice will profit by reading this useful and stimulating work.

The Intervertebral Discs. By ORMOND A. BEADLE. A special report issued by the Medical Research Council. Pp. 79, Figs. 47. London: H.M. Stationery Office. Price 2s.—For many years past Professor Schmorl in Dresden has made an intensive study of the anatomy and pathology of the spine, with especial regard to static deformities. Over 7,000 spines have been removed post-mortem and sectioned, and over 600 of these put up as permanent museum specimens. As a result of all this patient investigation there has come to our knowledge the facts relating to the variations to which the intervertebral discs are subject, both in health and disease. The most remarkable of these abnormalities is the enlargement of the central part of the pulpy disc and its fungation, as it were, into the cancellous tissue of the adjacent vertebræ. The author of the present monograph has done a great service to English readers by putting together in a convenient form

these researches of Schmorl. Of very great value is the series of forty-seven plates, which give a beautiful representation of the naked-eye and microscopic anatomy of the spine and its discs.

An Outline of Medicine for Nurses. By JAMES FARMING, M.D., D.P.H. Pp. 136. Bristol: John Wright & Sons, Ltd. 1933. Price 2s. 6d. — This small book is essentially a condensation product. It contains a large amount of useful information well presented; but necessarily suffers from some of the defects associated with an attempt to include too much in a small space. The chapter on heart disease in particular appears inadequate and too brief to be useful. A similar criticism applies to the section on anæmia, particularly pernicious anæmia, which contains no mention of subacute combined degeneration or achlorhydria. Respiratory diseases are much better done, though a notable omission is found in the absence of any reference to the treatment of hæmoptysis. Alimentary disorders are well done. There is a useful chapter on infant feeding and on the dietary of children, though four-hourly breast feeding is not mentioned. Renal and nervous diseases are adequately treated in the small space available. The book is useful as a guide to anyone who is called upon to lecture to nurses and who has to pay attention to the standard syllabus.

Neurological Effects of Syphilis. By B. B. SHARP, M.D. Pp. viii., 92. Illustrated. London: Oxford University Press. 1933. Price 7s. 6d.—This little volume contains an interesting and readable account of neurosyphilis, in its pathological and therapeutic aspects. Most of the modern work on the morbid anatomy has been incorporated. A detailed description is given of the various lines of treatment, but enthusiasm for new methods seems to have squeezed out any recognition of mercury as a therapeutic agent. The book is entirely a compilation and bears no trace of original observation or research work; there is, moreover, a paucity of critical comment. Its object and scope are not easy to determine.

Obituary

WILLIAM ALEXANDER SMITH, M.A., M.B., M.R.C.S., F.C.S.

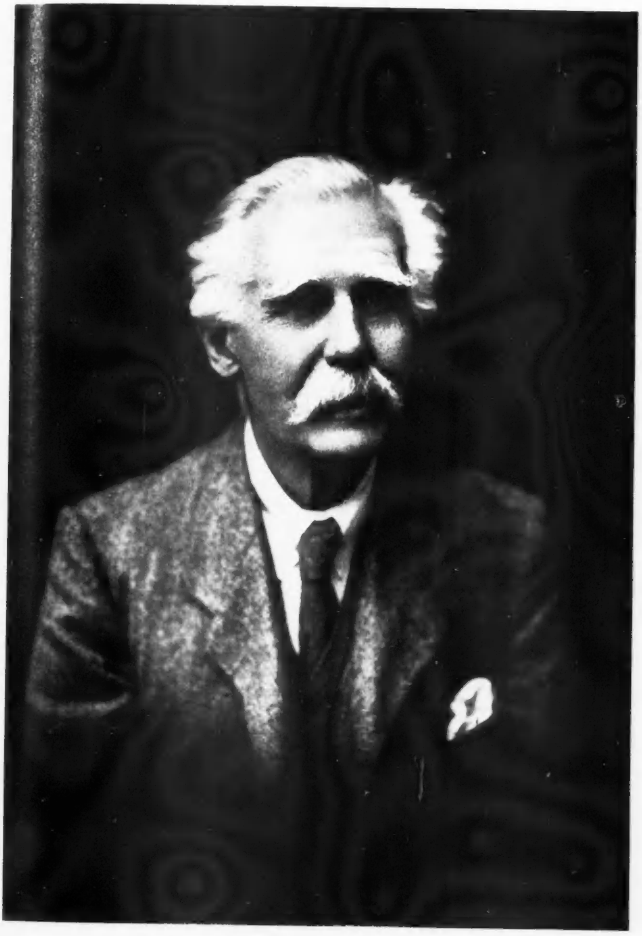
Dr. William Alexander Smith was born on August 9th, 1852, at Chesterfield, Derbyshire. His father, Dr. William Smith, after qualifying at the new Bristol School and practising for a time in Park Street and elsewhere, had settled in Chesterfield and been appointed Surgeon to the Hospital. Thus his eldest son "Sandy" came to begin his education in the Chesterfield Grammar School. He next went to a Quaker School under Messrs. Tilden and Smith at Weston-super-Mare. When the father returned to Clifton and built No. 70 Pembroke Road as his home, his son entered Clifton College under Dr. Percival in 1867. He rose to the Sixth, distinguishing himself in chemistry, but also gaining those literary and classical tastes which pervaded all his later life.

On leaving in 1872, he went, after winning an entrance studentship, to Christ Church, Oxford, and finally got First Class Honours in the Natural Science Schools of 1875. At St. Mary's Hospital he took the highest place in the scholarship competition, and qualified in 1880 as M.A., M.B., M.R.C.S., to which he added the F.C.S.

He chose to engage in country practice, and settled down at Newport in Essex, where he was ere long made Surgeon to the Saffron Walden Hospital near there. He had to travel long distances in his dogcart or on horse-back, and thoroughly did he enjoy his open-air life. Even here he got together a little club of friends, a reading society of twelve members, the Duodecimos.

He married Mary Catherine, a daughter of Mr. Mark Whitwill of Bristol, by whom he had one girl, afterwards Mrs. Clover. His wife dying in 1907, he returned to Clifton, practised for a time in Durdham Park, and later on joined his sisters in the family house, 70 Pembroke Road.

When the Panel Referee was called up for war service Dr. Smith was chosen to succeed him, and he did much good



WILLIAM ALEXANDER SMITH.

work of the same kind for the Pensions Board and afterwards under the Insurance officials. He also served this *Journal* for a time during the war as Editorial Secretary.

Besides these duties he had many other interests. He was Secretary of the Shakespeare Society, Chairman of the Research Defence Society, and Treasurer of the Naturalists. Again, besides collecting a marvellous library of his own, he gave much time to helping Mr. C. K. Rudge to discover and sort out the rare volumes among the books of the Medical Library.

When Mr. Rudge died in 1926 he was elected Hon. Medical Librarian. From henceforward he worked assiduously for the Library, searching out and recommending the works needed and making critical lists of the new books and editions with the skill of a booklover and of a ripe scholar.

After five years' service for the Library he was suddenly taken ill at the end of a long day of his referee work. He rallied, but had to give up all his activities. At last, in November, 1932, he moved to Cambridge, to be with his daughter and his grandchildren. For a time he lived happily enough, but a relapse came on and ended fatally on August 3rd, 1933. As a friend described him: "Tall, shaggy, silvery-haired, stooping, uncoated in the coldest weather, with an endearing hesitancy of speech, there was lost to us the figure we loved."

CHARLES ALBERT CALMETTE.

"A PERSONAL TRIBUTE TO HIS MEMORY."

BY

PROFESSOR S. L. CUMMINS, C.B., C.M.G., M.D.,

David Davies Professor of Tuberculosis,
Welsh National School of Medicine.

READERS of *The Bristol Medico-Chirurgical Journal* will have seen the numerous obituary notices of the late Dr. Charles Albert Calmette which have appeared in the Press. It is, therefore, unnecessary to refer at length to his younger days spent as a naval surgeon in Chinese waters or to his first entry into independent scientific study as a young bacteriologist picked out by Pasteur for special work at Saigon. It was

there that he made his earliest contributions to preventive medicine and obtained world-wide renown for his researches on snake venom and their treatment by specific anti-sera. What may, perhaps, be of some interest is a personal account of a charming French gentleman, who was also one of the greatest medical scientists of our time.

My first encounter with Calmette was in the town of Lille the week after the Germans had been driven from it in the autumn of 1918. Having recently taken over the duties of Adviser in Pathology to the British Forces in France from Sir William Leishman, it was my duty to keep in touch with the mobile laboratories as our troops pushed forward; and so I hurried up to Lille partly to enjoy the opportunity of meeting Calmette, already well-known to me by reputation, and also to ask for his help in case any of our laboratory units were in his neighbourhood. I found, however, that Major Fitzgerald, of the Canadian Army Medical Corps (now the Director of the Connaught Laboratories at Toronto), had already, on his own initiative and with Calmette's kind consent, installed his mobile laboratory in the Pasteur Institute at Lille, and had received every possible courtesy and help from its distinguished Director. It was wonderful to meet this renowned scientist, still at his post in spite of the German invasion, and now once more amongst friends and Allies at the end of his long ordeal.

Where a pathologist of world-wide reputation, controlling an institution of international value, might have expected nothing but courtesy and co-operation even from a foe, Calmette had been exposed to many indignities and hardships even by men whom he had known as colleagues in pre-war days. His beloved wife had actually been taken away into Germany as a hostage, where she was kept for months incarcerated with a number of other detained women, some of undesirable character, for no crime at all, except that of being a French lady of distinction. Yet, in spite of all these things, there was no inveterate rancour or bitterness in the heart of Calmette; and he exhibited with gaiety as well as pride the last rabbit which he had been permitted to preserve for the maintenance of the rabies virus.

Our next encounter was in Paris, after he had assumed the post of Assistant Director of the Pasteur Institute under Dr. Roux. He was no longer the tired leader of a forlorn hope, as he had seemed at Lille, but now he stood resplendent in the smart uniform of a Surgeon-General in the French

Army. His kindness and his affability, however, were in no way diminished. No holder of a distinguished position was ever more approachable, helpful and kind. At the Conference of the International Red Cross Society, held at Cannes in the Spring of 1919, Calmette was present as one of the Mission of French Scientists delegated to attend. It was a time when the attitude of many of us towards our late enemies was still embittered; and yet Calmette, who had suffered deeper personal trials than any, showed a real sense of the importance of re-establishing the bonds that should unite doctors across national frontiers in the world-wide conflict with disease. When, at a later date, it was my privilege to be appointed Professor of Tuberculosis in the University of Wales, I had frequent occasions to maintain personal touch with Dr. Calmette. It was then that I came to recognize fully the unequalled value of this great specialist in relation to tuberculosis.

Perhaps it may be permissible to speak a few words on this subject.

The contributions of Calmette to the study of tuberculosis and to its prevention have been on a scale unequalled by any individual worker since Robert Koch. Villemin, an army doctor, had been the first to demonstrate clearly the transmissibility of tuberculosis from man to animals and from one animal to another, thus proving its infective nature; and Calmette, a naval medical officer, was amongst the pioneers in following up this problem of infectivity, with a view to its prevention on scientific lines. The first objective was clearly to map out the distribution of infection, as opposed to disease, in human aggregations. Simultaneously with Wolff-Eisner, and independently of him, Calmette published in June, 1907, the first account of an ophthalmo-reaction, demonstrating that the application of diluted tuberculin to the conjunctiva could elicit, in sensitive persons, a marked inflammatory response of a specific though transitory kind. This discovery, published within a month of Von Pirquet's first announcement of his cutaneous test, was destined to be widely used for a short period, but it proved dangerous in certain cases, and Calmette himself was amongst the first to advocate the safer Von Pirquet technique as the best method for working out the distribution of infection in different racial groups and at varying age periods. He did not, however, stop short at the mere publication of a good method. Instead, he threw himself into a laborious propaganda for the use of cutaneous

tuberculin tests in the native populations throughout the French Colonies, and with the help of the Pasteur Institutes in the Colonies was instrumental in accumulating a vast mass of evidence as to the state of tuberculization of the natives of French Africa, Indo-China and other French Dependencies from 1911 onwards.

Still another contribution was already under way. During the years of trial at Lille Calmette had not been idle. It was during those years that he built up from existing literature the wonderful book which has, perhaps, done more than any other publication to spread through the world scientific conceptions of tuberculosis. The first publications of "L'Infection Bacillaire et la Tuberculose chez l'Homme et chez les Animaux" appeared in 1919. His object in writing it was, in his words, "to gather together from the most important works on tuberculosis since the publication of Straus's book in 1895," and from his personal researches, "the scientific principles on which, in the actual state of our knowledge, should be based the fight against the most terrible infectious disease from which humanity suffers." It is impossible to contemplate this book without admiration for the industry, accuracy and determination required to bring it to fruition. Its reception by the medical profession is a good index of its worth. The first (1919) and second (1922) editions were rapidly sold out, and the third (1927), a still more comprehensive work, is always in great demand amongst students of tuberculosis.

Finally came his greatest experiment, the inception of an attempt at tuberculosis prevention on lines peculiarly suitable to a follower of Pasteur—the use of a living attenuated virus, B.C.G., as a vaccine against tuberculosis. With his colleague Guèrin Calmette had worked for sixteen years at the attenuation of a bovine strain of tubercle bacillus handed him at its full virulence by the veterinary bacteriologist Vallée. Calmette had formed the opinion that ox bile, while not interfering with the growth of tubercle bacilli, might possess the property of reducing their virulence by its physical action on the fatty and waxy constituents of cultures, and it was through successive cultivations of this strain on bile-potato medium that attenuation was at last successfully brought about, until a stage was reached when the virulence for laboratory animals had diminished almost to vanishing point. It was now safe to attempt experiments on human beings, and his trusted colleagues, Weill-Hallé and Turpin,

took the next step—the feeding of this vaccine to infants in their earliest days, at a time when the permeability of the intestine was at its maximum and the tissues not yet hypersensitive through infection. The earliest vaccinations were carried out between 1921 and 1924, and it was soon clear that the vaccine was innocuous in the doses used. Since that time the use of B.C.G. has grown to enormous proportions throughout France and her Colonies, as well as in many parts of Europe and America. England alone has held aloof.

In 1927, the Medical Research Council gave close attention to the possibility of a controlled test on children in this country, and it was my lot to be sent to Paris to discuss the question with Professor Calmette and report. As a result of this visit a programme was formulated, based on the use of an adequate amount of vaccine supplied by the Pasteur Institute, to be given to selected children living in contact with "open" cases, under conditions where close supervision might be carried out during subsequent months and years. With characteristic courtesy, Calmette at once promised to supply all the vaccine required free of charge.

The statistics quoted in France had been subjected, however, by Professor Major Greenwood and others to rather damaging criticism, not with regard to the innocuity of the vaccine, which was admitted, but as to its utility in the doses used and when given by the mouth. Under these circumstances, the Medical Research Council decided that no official test on children was desirable until further experiments on monkeys and other animals had been carried out for the Council by Dr. Stanley Griffith. This delay was a great disappointment to Calmette. Writing to me in 1930, he could not refrain from a sly dig at the Labour Government then in office! "Je sais que votre Gouvernement, malgré son étiquette travailliste, est le plus conservateur qui soit au monde, mais il me semble tout de même qu'il finira par comprendre qu'il est de son intérêt de ne pas se priver d'un moyen efficace et inoffensif de combattre la tuberculose."*

In a postcript to the same letter he refers amusingly to a much advertised non-medical producer of vaccines and serums against tuberculosis in the neighbouring country of

* "I know that your Government, in spite of its Labour label, is the most conservative in the world, but it seems to me all the same that it will realize in the long run that it is to its interest not to deprive itself of an effective and innocuous weapon for combating Tuberculosis."

Switzerland, "qui parait trouver, auprès des autorités officielles britanniques, une certaine complicité et une bienveillance qu'il nous serait agréable de voir accorder aussi à nos travaux ! "*

The Lübeck disaster came as a terrible set-back to the use of B.C.G. throughout the world; but the attitude of some scientists amongst our late enemies was a great comfort and support to Calmette, and he sent me, with obvious pleasure, a copy of a noble letter which he had received from Dr. E. Altstaedt, one of those convicted at the trial at Lübeck, written in most generous terms, entirely exonerating Calmette from any responsibility for the disaster and finishing in the following words :—

> "The judgement of Lübeck is pleasant at least in the sense that it has resulted in the official proof of a contamination."

The Lübeck tragedy and the subsequent trial had involved mental anguish to Calmette, and it is doubtful if his bodily health ever quite recovered from the strain. Even the final judgement was insufficient to remove the impression of danger which the disaster had fostered in the minds of some of those who might have contemplated the use of the vaccine, and its world-wide use has undoubtedly become limited as a result.

It is, perhaps, still too early to decide whether the claims for B.C.G. are to be accepted in full, but its innocuity is proved; and the recent work of Dr. A. Stanley Griffith and Professor J. B. Buxton at Cambridge has demonstrated beyond question that by its means calves can be given an almost complete protection against large doses of virulent bovine tubercle bacilli.

It is quite certain that the vast experiment undertaken by Calmette represents one of the most important, as well as the most courageous, investigations ever initiated into the problem of prevention of tuberculosis. Whether it may prove as successful as Calmette had hoped, or whether other inoculation methods, safer and more efficient, may be found in the future, the vast B.C.G. experiment must necessarily result in a great increase of our knowledge about the responses of the body to infection with tubercle bacilli.

In the death of Calmette medical science has lost one

* "Who appears to find among British Government Officials a sort of complicity and goodwill which it would be very pleasing to see extended to our own work."

of its foremost investigators. To those who had the privilege of his friendship the loss is still deeper. Humanity has no more delightful representative than a cultured, witty and intelligent Frenchman. All these qualities were exhibited in their finest form in Charles Albert Calmette.

Meetings of Societies.

Bristol Medico-Chirurgical Society.

SESSION 1932–33.

THE Annual General Meeting of the Society was held at the University on Wednesday, 11th October, 1933, at 8.30 p.m.

Dr. J. R. Charles was in the Chair until the arrival of the President, and seventy-eight members were present.

The Hon. Secretary read his report for the past year, and Mr. E. Watson-Williams read the annual report of the Hon. Editor of the *Journal*. These reports were adopted, and the Hon. Secretary and the Hon. Editor thanked for their work.

Dr. Carleton then proposed that Professor A. Rendle Short should be elected as President-Elect. This was seconded by Mr. Duncan Wood, and carried with acclamation.

Mr. Jackman proposed and Mr. E. Watson-Williams seconded that Mr. Shepherd should be re-elected as Hon. Secretary. This was carried. Dr. George Parker was unanimously re-elected as Hon. Medical Librarian on the proposition of Mr. E. Watson-Williams and seconded by Dr. Gee.

Dr. Frank Bodman proposed and Dr. Perry seconded that the following nine gentlemen be elected as members of the Committee :—

Dr. Carleton.	Dr. A. L. Flemming.
Dr. Elwin Harris (jun.).	Dr. H. L. Fuller.
Mr. Jackman.	Dr. P. C. Martin.
Mr. Clifford Moore.	Dr. Vincent Wood.
Mr. Duncan Wood.	

BRISTOL MEDICO-CHIRURGICAL SOCIETY.

INCOME AND EXPENDITURE ACCOUNT for the year ended 30th September, 1933.

INCOME.	£ s. d.	£ s. d.
Members' Subscriptions ..	330 4 6	
Do., outstanding for 1932–1933	51 19 6	
		382 4 0
Interest on Bank Deposits		2 17 3
Interest on £500 4 per cent. Consolidated Stock, less tax		15 0 0
		£400 1 3

EXPENDITURE.	£ s. d.	£ s. d.
Grant to *The Bristol Medico-Chirurgical Journal*		230 15
Librarian—Honorarium		15 0
Miscellaneous Expenses—		
Goodway–Refreshments	16 0 0	
Postages and Sundries	8 7 6	
Printing and Stationery	12 15 0	
Audit Fee	2 2 0	
Lantern and Cinematograph at Meetings ..	6 6 0	
W. Jewell—rehanging and reframing portraits	4 12 0	
University Marshal ..	1 0 0	
Lewis's Medical and Scientific Library—		
£ s. d.		
Subscription 4 4 0		
Postages .. 0 16 7		
	5 0 7	
		56 3
		301 18
Balance, being excess of Income over Expenditure for the year, carried to Balance Sheet		98 2
		£400 1

BALANCE SHEET as at 30th September, 1933.

LIABILITIES AND CAPITAL.	£ s. d.	£ s. d.
Sundry Creditors		13 14 2
Capital as at 30th Sept., 1932	680 1 6	
Add Surplus on Income and Expenditure Account as above ..	98 2 8	
		778 4 2
		£791 18 4

ASSETS.	£ s. d.	£ s. d.
Cash at Bank—		
Current Account	138 16 1	
Deposit Account	163 13 9	
		302 9
£500 4 per cent. Consolidated Stock at cost		437 9
Sundry Debtors—		
Members' Subscriptions for 1932–1933 outstanding ..		51 19
		£791 18

Audited and found correct,
H. E. KEELER,
Chartered Accountant
Auditor.

16-18 Clare Street, Bristol 1,
10*th October*, 1933.

Dr. Phillips proposed and Dr. Zealand seconded that the following three members be elected to serve on the University Library Sub-Committee: Dr. G. Parker, Dr. Elwin Harris (sen.), Dr. Symes.

The Hon. Secretary then spoke of the Society's Annual Dinner, and a Dinner Committee was elected consisting of the President, Mr. Jackman and the Hon. Secretary.

The President, Mr. Hey Groves, then arrived, and after thanking Dr. Charles took the Chair. He proceeded at once to resign his office to his successor, Dr. Elwin Harris (sen.). A vote of thanks to the retiring President was proposed by Mr. Jackman and seconded by Dr. Elwin Harris (jun.). This was carried with acclamation.

The President then gave his inaugural address.

A vote of thanks to the President for his address was proposed by Mr. Carwardine and seconded by Mr. Chitty, and carried with acclamation.

The Hon. Treasurer then read his report for the past year. The report was adopted, and the Treasurer thanked for his work. Mr. Iles was re-elected Hon. Treasurer on the proposition of Mr. Wright, seconded by Mr. Clifford Moore.

The second meeting of the session was held at the University on Wednesday, 8th November, 1933, at 8.30 p.m.

Dr. ELWIN HARRIS was in the Chair, and fifty-eight members were present.

Dr. A. L. TAYLOR and Dr. T. B. WANSBROUGH showed pathological specimens and skiagrams respectively.

The minutes of the Annual Meeting were read and confirmed.

Professor R. S. S. STATHAM then read a paper on **"Vaginal Discharge."**

A discussion then followed, in which Mr. SMYTHE, Mr. SHEPHERD, Mr. WALTERS and the PRESIDENT spoke. Professor STATHAM replied, and at his request Dr. A. D. FRASER spoke on the pathology of the problem.

The third meeting of the session was held at the University on Wednesday, 13th December, 1933, at 8.30 p.m.

Dr. ELWIN HARRIS was in the Chair, and forty-nine members were present.

Dr. BERGIN and Dr. FRASER showed X-rays and pathological specimens respectively.

Mr. E. WATSON-WILLIAMS showed a rhinolith removed at operation.

The question of the times of meetings was again read, and after the Hon. Secretary had explained the situation and several members had spoken in favour of continuing the later hour, the PRESIDENT made a proposition from the Chair that the meetings should continue to be held at 8.30 p.m. This was carried unanimously.

The PRESIDENT then called on Professor J. A. NIXON, who read a paper entitled **"The Recognition of Inherited Syphilis."** A long and interesting discussion followed, in which the PRESIDENT, Dr. RICHARD CLARKE, Dr. CHARLES, Dr. BIRRELL, Dr. GEE, Dr. FRANK BODMAN, Dr. ALEXANDER, Dr. GARDEN, Mr. FITZGIBBON, Mr. SHEPHERD, and Mr. E. WATSON-WILLIAMS spoke, and Professor NIXON replied.

The Medical Library of the University of Bristol,

WITH WHICH IS INCORPORATED

The Library of the Bristol Medico-Chirurgical Society.

The following donations have been received since the publication of the list in June, 1933.

November, 1933.

American Laryngological Association (1) ..	1 volume.
British Hanovia Quartz Lamp Co. Ltd. (2) ..	1 ,,
Carnegie Institution of Washington (3) ..	1 ,,
Granada University (4)	1 ,,
Professor E. W. Hey Groves (5)	1 ,,
Dr. Jonas (6)	1 ,,
Otago University (7)	1 ,,
Purcell Research Memorial (8)	1 ,,
Rockefeller Foundation (9)	1 ,,
Royal College of Surgeons of England (10) ..	1 ,,
Professor R. S. S. Statham (11)	1 ,,
Wilmer Institution of the Johns Hopkins University (12)	1 ,,
John Wright & Sons Ltd. (13)	1 ,,

Unbound periodicals have also been received from Professor E. W. Hey Groves.

THE ONE HUNDRED AND FORTY-FIFTH LIST OF BOOKS.

The figures in round brackets refer to the figures after the names of the donors. The books to which no such figures are attached have either been bought from the Library Fund or received through the *Journal*.

Abrahams, A. .. .. *Diseases and Disorders of the Digestive Organs* 1932

Actinotherapy Technique .. .. (2) [1933]

Beaumont, G. E. .. *Medicine: Essentials for Practitioners and Students* 1932

Berry, R. J. A. .. .. *Stoke Park Studies, Series* 1. *Mental Deficiency* 1933
Bickerton, J. M., and Savin, L. H. *Clinical Ophthalmology* 1933
Blacklock, D. D. .. *Empire Problem* 1932
Bostock, J. .. .. .. *Neural Energy Constant* 1931
Brain, W. R. .. .. *Diseases of the Nervous System* 1933
Buchanan, A. .. .. *Midwifery Mechanics* .. .. (11) N.D.
Cameron, A. J. D. .. *Some Thoughts on Asthma* 1933
Charles, E. .. .. .. *Practice of Birth Control* 1932
Clay, H. H. .. .. *Sanitary Inspector's Handbook* 1933
Combe, A. .. .. *Principles of Physiology* .. .. 5th Ed. 1836
Core, D. .. .. .. *Examination of the Central Nervous System* 1928
Crocket, J. .. .. *Physical and Radiological Examination of the Lungs* .. .. 2nd Ed. 1931
Devine, H. .. .. *Recent Advances in Psychiatry* 1929
Douthwaite, A. H. .. *Treatment of Rheumatoid Arthritis and Sciatica* .. .. 2nd Ed. 1933
Ellis, Havelock .. *Psychology of Sex* 1933
Ellman, P. .. .. *Chest Disease in General Practice* 1932
Fanning, J. .. .. *Outline of Medicine for Nurses* 1933
Fuller, E. .. .. .. *On the Management of a Birth Control Centre.* 2nd Ed. [1931]
Gallichan, W. M. .. *Critical Age of Women* 1932
Goodwin, F. .. .. *Account of the Neutral Saline Waters at Hampstead* 1804
Gordon, R. G. .. .. *Neurotic Personality* 1927
Gordon, R. S., and Brown, M. F. *Paralysis in Children* 1933
Gourmont, R. de .. *Natural Philosophy of Love* 1926
Groves, E. W. H. .. *Surgical Operations* 1933
Groves, E. W. H. .. *Synopsis of Surgery* .. .. 10th Ed. 1933
Hall, P. .. .. .. *Ultra Violet Rays* .. .. .. 4th Ed. 1929
Ham, B. B. .. .. *Handbook of Sanitary Law* .. 11th Ed. 1931
Hare, D. C. .. .. *Simple Instructions for Diabetic Patients* .. 1933
Harington, C. R. .. *Thyroid Gland* 1933
Harris, R. W., and Sack, L. S. *Medical Insurance Practice.* 3rd Ed. 1929
Herelle, F. D' .. .. *Bactériophage et son Comportement* 1926
Herries, N. E. .. .. *Guide to Birth Control Literature* 1931
Hindley-Smith, T. D. *Chronic Rheumatism and the Pre-Rheumatic State* 1932
Hobhouse, N. .. .. *Nervous Disorders in Infancy and Childhood* 1932
Hunt, T. C. .. .. *Common Causes of Chronic Indigestion* 1933
James, R. R. .. .. *Studies in the History of Ophthalmology in England prior to* 1800 1933
Jones, H. E. .. .. *Practical Points in Eye Surgery and Dressing* 1933
Kemble, J. .. .. *Idols and Invalids* .. .. [1933]

Kidd, ... *Common Infections of the Female Urethra and Cervix* 1929
M'Cabe, J. .. .. *Observations on the Cheltenham Waters* .. 1820
McConnel, J. K. .. *Adjustment of Muscular Habits* 1933
Martin, C. R. A. .. *Practical Food Inspection* Vol. II. 1933
Massie, G. .. .. .. *Surgical Anatomy* 1928
Ministry of Health .. *Final Report of Departmental Commission on Maternal Mortality and Morbidity* 1932
Morison, J. .. .. *Bacteriophage in Treatment and Prevention of Disease* 1932
Mouth Infections and their Relation to Systemic Disease. Vol. 2 .. (8) 1933
Mozo, F. G. .. .. *Fisiopatologia del Metabolismo basal* .. (5)
Muir, R. .. .. .. *Textbook of Pathology* .. .. 3rd Ed. 1933
Norske Medicinske Selskab. 1833-1933. *Festskrift* 1933
Pasteur (*Oeuvres de*) .. *Tomes V et VI* 1928-1933
Power, D'Arcy .. .. *Short History of Surgery* 1933
Read, G. D. .. .. *Natural Childbirth* 1933
Schola Medicinae Bristol. 1833-1933 .. .. (13) 1933
Sewart, D. .. .. *Liver Diet Cookery Book* 1933
Shattuck, G. C. .. *Peninsula of Yucatan* .. .. (3) 1933
Smith, R. W. I. .. *English Speaking Students of Medicine at the University of Leyden* 1932
Spira, L. .. .. .. *Clinical Aspect of Chronic Poisoning by Aluminium and its Alloys* 1933
Stevens, W. M. .. .. *Resistance to Disease* 1933
Treatise on Cold Mineral Waters 1766
Walker, G. F. .. .. *Injured Workman* 1933

TRANSACTIONS, REPORTS, JOURNALS, ETC.

American Laryngological Association. Transactions of the 54th Annual Meeting .. .. (1) 1932
Boletin de la Universidad de Granada. Ano IV. No. 21 .. (4) 1932
Collected Papers of the Mayo Clinic and the Mayo Foundation. XXIV. 1932
College of Physicians of Philadelphia, Transactions. Vol. 54.. .. 1932
Medical Annual 1933
Medical Society's Transactions. Vol. VI. 1933
Otago University Medical School, Proceedings. No. 10 .. .. (7) 1933
Rockefeller Foundation, Annual Report .. .. (9) 1932
Royal College of Surgeons of England. Calendar .. .. .. (10) 1933
St. Thomas's Hospital Reports. Vol. LV. 1931
Surgical Clinics of North America. Vol. 13. Nos. 2, 3 and 4 .. 1933
Wilmer Ophthalmological Institute, Collected Reprints. Vol. 111 (12) 1933

Publications Received

From THE ACTINIC PRESS :

Therapeutic Uses of Infra-Red Rays. 2nd Edition. By W. A. TROUP, M.C., M.B., Ch.B. Price 6s. 6d.

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British Journal of Surgery. Vol. XXI. Nos. 81, 82. 1933. Price 12s. 6d. each.

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Miner's Nystagmus. By F. O'SULLIVAN, M.B., Ch.B., B.A.O. Price 5s.

Local Medical Notes

EXAMINATION RESULTS.

University of Bristol.—Students of the University have recently passed the following examinations:—

M.B., Ch.B.—*First Examination.*—P. A. Bennett, K. J. V. Carlson, A. A. K. Datta, M. Dworkis, W. H. G. Elliott, M. M. Lewis, Joan E. Mackworth, G. R. E. Maxted, J. S. Richardson, E. W. J. Townsend. *Physics:* Kathleen Byrt. *Chemistry:* Joyce S. Miller, K. Savill.

M.B., Ch.B.—*Supplementary First Examination.*—K. A. Hall, K. Savill.

M.B., Ch.B.—*Second Examination. Part I. Organic Chemistry:* K. J. V. Carlson, R. L. J. Derham, P. K. Jenkins.

M.B., Ch.B.—*Final Examination. Part I. (including Forensic Medicine and Toxicology):* V. T. Baxter (with distinction in Forensic Medicine and Toxicology), Kathleen G. Brimelow (with distinction in Forensic Medicine and Toxicology), F. C. Collingwood, Theodora M. Crabtree, J. G. Field, P. N. Heron, A. E. Jowett, S. D. Loxton (with distinction in Materia Medica and Pharmacy, Pharmacology and Therapeutics), A. W. Woolley (with distinction in Forensic Medicine and Toxicology).

M.B., Ch.B.—*Final Examination. Part II.:* S. B. Adams. *Group II.:* Frances E. Powell.

B.D.S.—*First Examination. Chemistry:* F. P. Ewens. P. H. S. Paine. *Physics:* J. C. Jowett.

B.D.S.—*Supplementary First Examination:* F. P. Ewens.

B.D.S.—*Second Examination. Anatomy and Physiology:* C. A. Blanden, C. C. B. Plumley.

L.D.S. — *Preliminary Science Examination. Biology:* H. W. Williams, M. J. Banbury, C. C. Moore.

L.D.S. — *Supplementary Preliminary Science. Physics and Chemistry:* J. F. Durie, C. C. Moore. *Biology:* J. B. Inverdale.

L.D.S.—*First Professional Examination. Anatomy and Physiology:* M. J. Banbury.

L.D.S. — *Second Professional Examination. Dental Mechanics and Dental Metallurgy:* B. E. Ffrench, Frances M. Orton, L. E. Scull, R. E. Buchan, D. E. Royal. *Dental Materia Medica:* J. G. Clancy.

Conjoint Board.—M.R.C.S., L.R.C.P.—*Chemistry:* R. T. Moore, A. C. F. Alexander. *Physics:* R. T. Moore. *Pharmacology and Materia Medica:* T. H. Taylor. *Pathology:* A. G. W. Branch, R. H. Moodie, J. N. Heales, R. A. Mathews, Dorothy E. Barber, Rosalind M. S. Derham. A. V. House.* *Medicine:* A. V. House,* W. R. Cambridge,* Winifred M. Hill,* E. O. Walker.* *Surgery:* D. A. J. Hunwick,* Gwladys R. Llewelyn, A. V. House,* W. R. Cambridge.* *Midwifery:* J. N. Heales, Dorothy E. Barber, Rosalind M. S. Derham, C. H. G. Price, Irene G. Hamilton. *Anatomy and Physiology:* E. J. Lace. *Physiology:* J. D. Buckner.

L.D.S., R.C.S.—*Final Examination. First Professional Examination. Part I. Dental Mechanics:* D. J. Dymond, W. White, *Part II. Dental Metallurgy:* J. T. S. Hutchins. *Part III. Anatomy and Physiology:* J. G. Jones.

L.D.S., R.C.S.—*Final Examination. Part I.:* T. H. Williams, G. L. R. Welch. *Part II.:* A. C. Davies,* D. Gent,* N. G. Harrison,* N. E. Miles,* H. F. Vere,* O. F. Harley, J. D. Rees.

* Qualified.

Society of Apothecaries of London.—L.S.A.—*Final Examination. Medicine and Midwifery:* G. C. Canaval.* *Surgery and Forensic Medicine:* G. C. Canaval.* *Medicine:* Helene L. Canaval.

* Qualified.

FIFTY-YEAR INDEX TO THE "JOURNAL."

It has, unfortunately, proved impossible to complete this in time for inclusion with the present issue. It will be sent to subscribers as soon as it is ready.

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